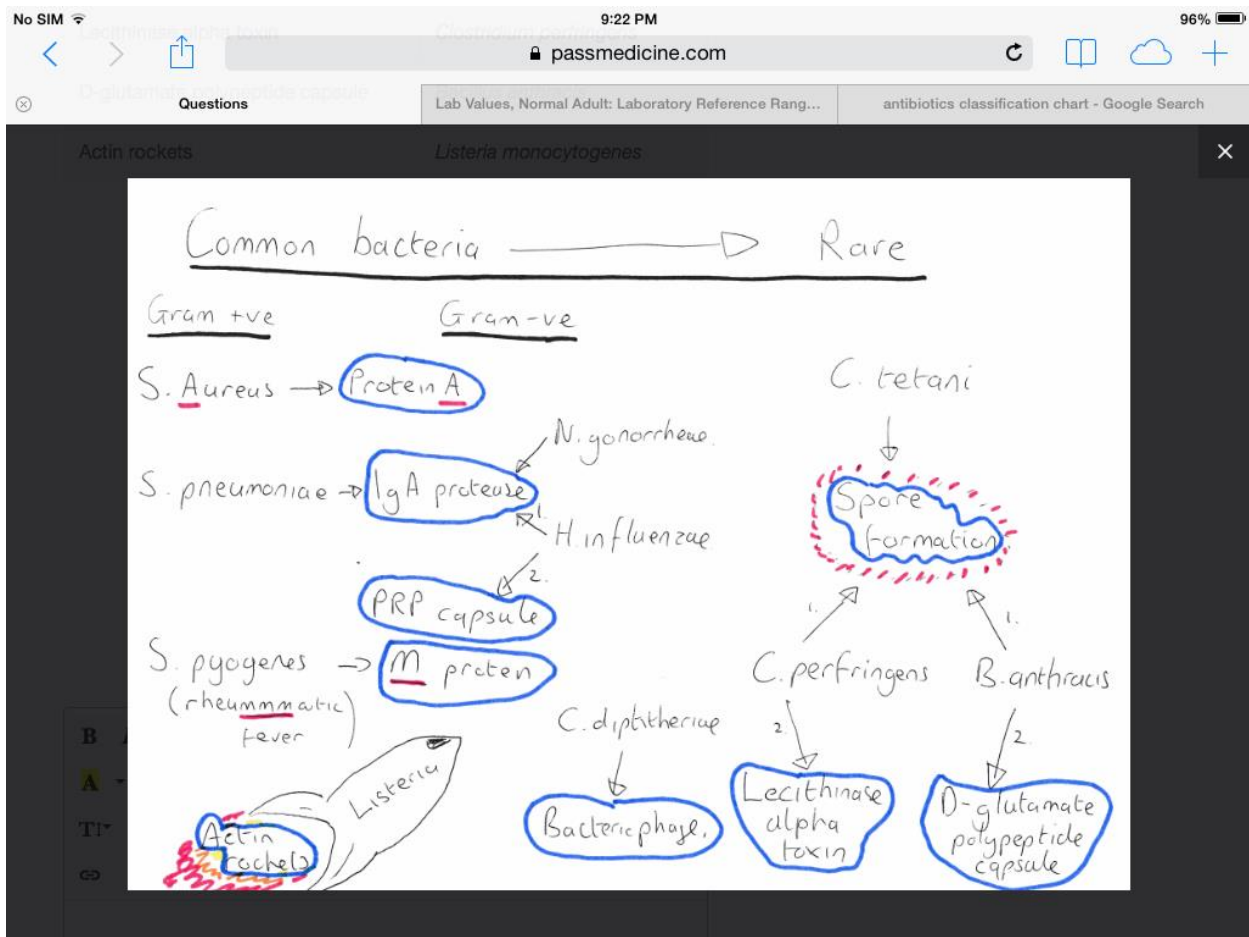

Virulence factors

Bacteria employ a large number of virulence factors which enable them to colonize the host and evade/suppress the immune response. The table below shows a select number of virulence factors which are important for the exam.

Virulence factor	Example organisms
IgA protease	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Neisseria gonorrhoeae</i>
M Protein	<i>Streptococcus pyogenes</i>
Polyribosyl ribitol phosphate capsule	<i>Haemophilus influenzae</i>
Bacteriophage	<i>Corynebacterium diphtheriae</i>
Spore formation	<i>Bacillus anthracis</i> <i>Clostridium perfringens</i> <i>Clostridium tetani</i>
Lecithinase alpha toxin	<i>Clostridium perfringens</i>
D-glutamate polypeptide capsule	<i>Bacillus anthracis</i>
Actin rockets	<i>Listeria monocytogenes</i>

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Classification of bacteria

Remember:

- Gram positive cocci = staphylococci + streptococci (including enterococci)
- Gram negative cocci = *Neisseria meningitidis* + *Neisseria gonorrhoeae*, also *Moraxella*

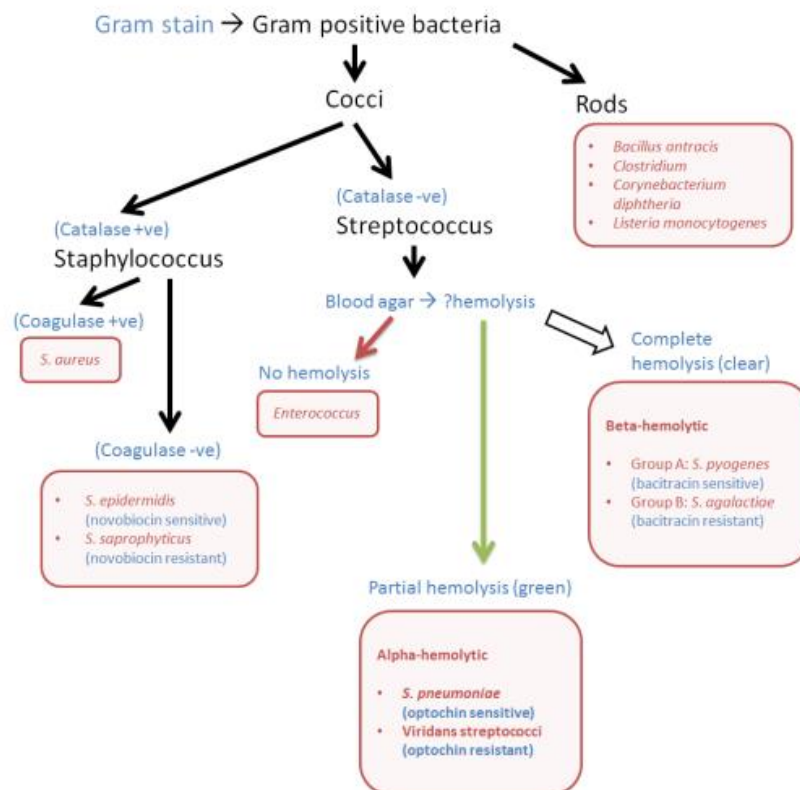
Therefore, only a small list of Gram positive rods (bacilli) need to be memorised to categorise all bacteria - mnemonic = ABCD L

- *Actinomyces*
- *Bacillus anthracis* (anthrax)
- *Clostridium*
- Diphtheria: *Corynebacterium diphtheriae*
- *Listeria monocytogenes*

Remaining organisms are Gram negative rods

Identifying gram-positive bacteria

Gram positive bacteria will turn purple/blue following the gram staining. Microscopy will then reveal the shape, either cocci or rods.



Rods (bacilli)

- *Actinomyces*
- *Bacillus anthracis*
- *Clostridium*
- *Corynebacterium diphtheriae*
- *Listeria monocytogenes*

Cocci

- makes catalase: Staphylococci

Rods (bacilli)

- *Actinomyces*
- *Bacillus anthracis*
- *Clostridium*
- *Corynebacterium diphtheriae*
- *Listeria monocytogenes*

Cocci

- makes catalase: Staphylococci
- does not make catalase: Streptococci

Staphylococci

- makes coagulase: *S. aureus*
- does not make coagulase: *S. epidermidis* (novobiocin sensitive), *S. saprophyticus* (novobiocin resistant)

Streptococci

- partial haemolysis (green colour on blood agar): α -haemolytic
- complete haemolysis (clear): β -haemolytic
- no haemolysis: γ -haemolytic

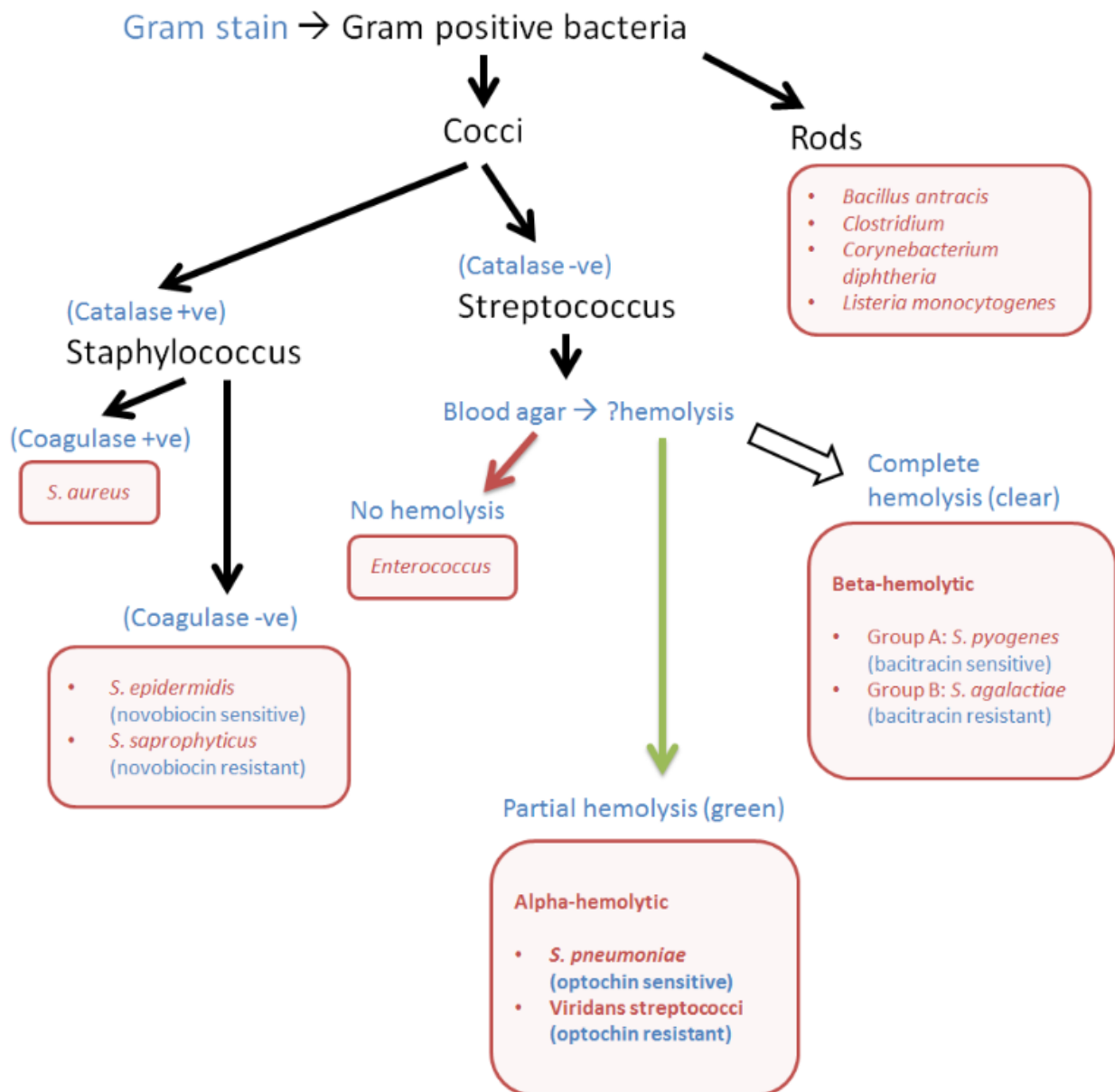
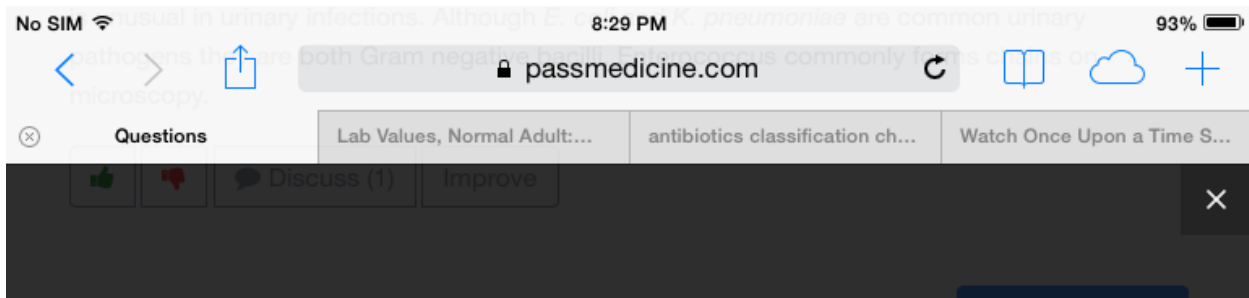
α -haemolytic streptococci

- optochin sensitive: *S. pneumoniae*
- optochin resistant: Viridans streptococci

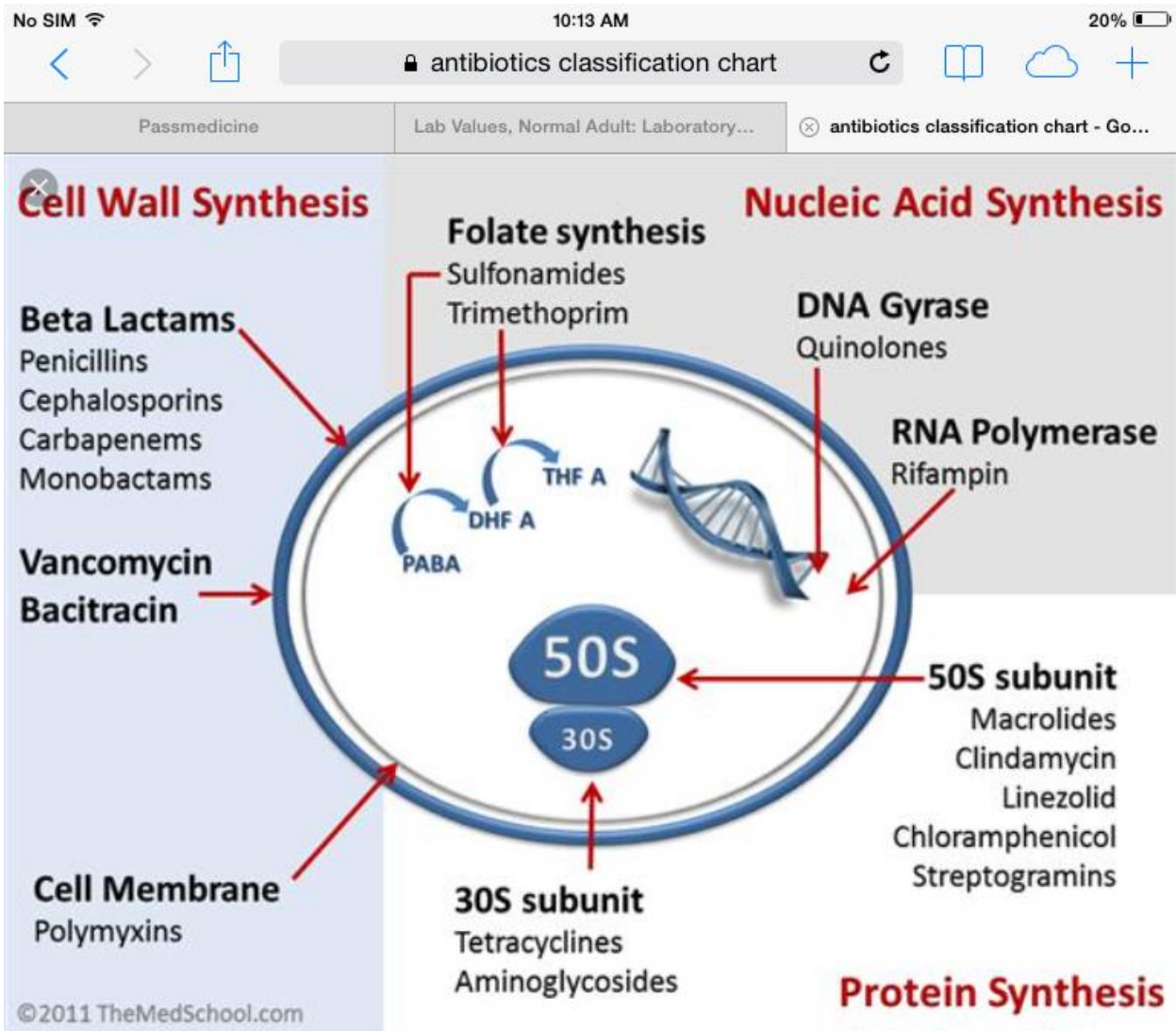
β -haemolytic streptococci

- bacitracin sensitive: Group A: *S. pyogenes*
- bacitracin resistant: Group B: *S. agalactiae*

Next question >



- *Actinomyces*
- *Bacillus anthracis*
- *Clostridium*
- *Corynebacterium diphtheriae*



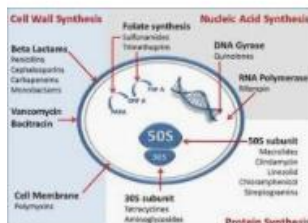
Orthobullets

Antibiotic Classification & Mechanism - Basic Science - Orthobullets

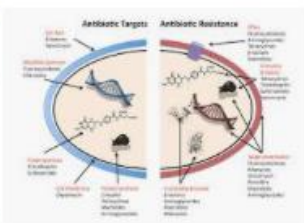
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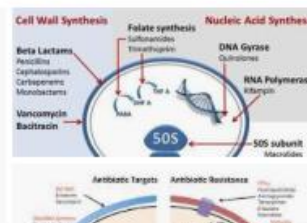
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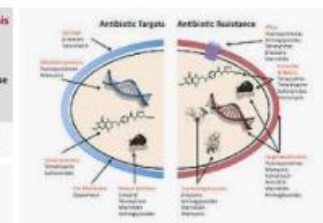
Antibiotics – Mechanisms of Action



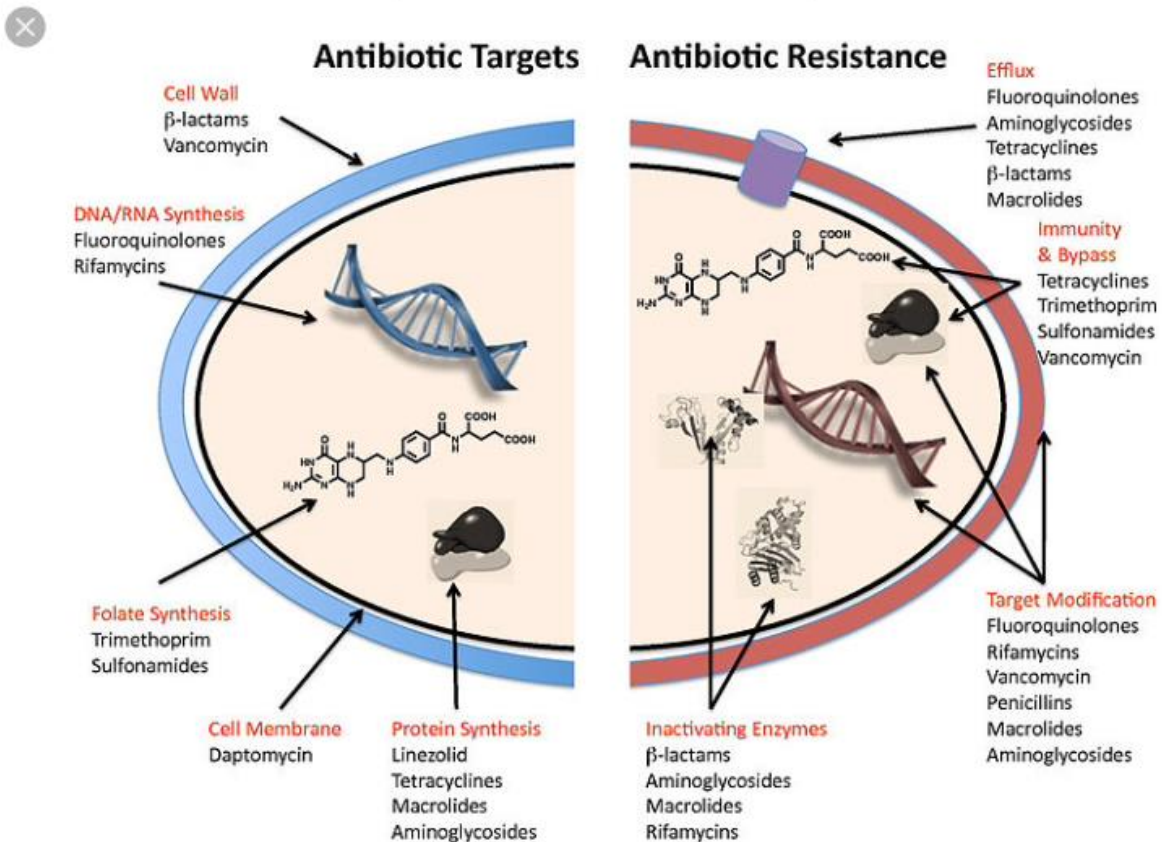
Antibiotic Targets



Antibiotic Resistance



Mechanism of action

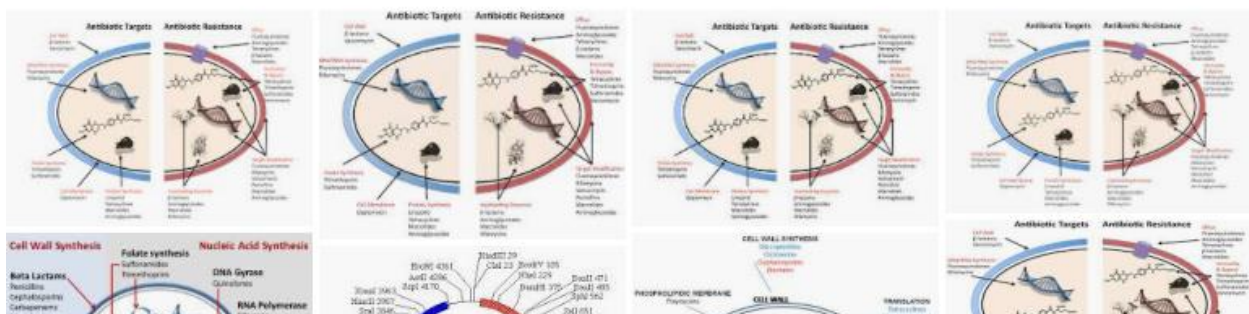


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Antibiotic guidelines

The following is based on current BNF guidelines:

Respiratory system

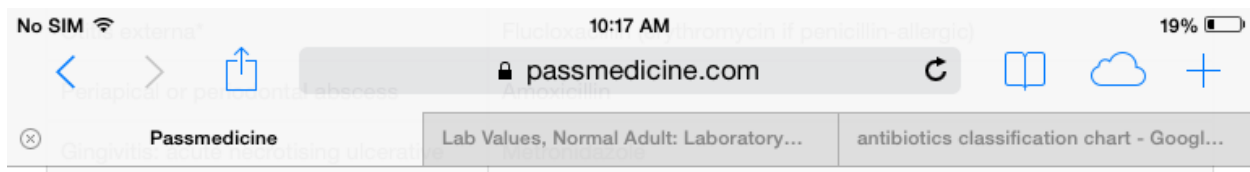
Condition	Recommended treatment
Exacerbations of chronic bronchitis	Amoxicillin or tetracycline or clarithromycin
Uncomplicated community-acquired pneumonia	Amoxicillin (Doxycycline or clarithromycin in penicillin allergic, add flucloxacillin if staphylococci suspected e.g. In influenza)
Pneumonia possibly caused by atypical pathogens	Clarithromycin
Hospital-acquired pneumonia	Within 5 days of admission: co-amoxiclav or cefuroxime More than 5 days after admission: piperacillin with tazobactam OR a broad-spectrum cephalosporin (e.g. ceftazidime) OR a quinolone (e.g. ciprofloxacin)

Urinary tract

Condition	Recommended treatment
Lower urinary tract infection	Trimethoprim or nitrofurantoin. Alternative: amoxicillin or cephalosporin
Acute pyelonephritis	Broad-spectrum cephalosporin or quinolone
Acute prostatitis	Quinolone or trimethoprim

Condition	Recommended treatment
Impetigo	Topical fusidic acid, oral flucloxacillin or erythromycin if widespread
Cellulitis	Flucloxacillin (clarithromycin or clindomycin if penicillin-allergic)
Erysipelas	Phenoxymethylpenicillin (erythromycin if penicillin-allergic)
Animal or human bite	Co-amoxiclav (doxycycline + metronidazole if penicillin-allergic)
Mastitis during breast-feeding	Flucloxacillin

Condition	Recommended treatment
Throat infections	Phenoxymethylpenicillin (erythromycin alone if penicillin-allergic)
Sinusitis	Amoxicillin or doxycycline or erythromycin
Otitis media	Amoxicillin (erythromycin if penicillin-allergic)
Otitis externa*	Flucloxacillin (erythromycin if penicillin-allergic)
Periapical or periodontal abscess	Amoxicillin
Gingivitis: acute necrotising ulcerative	Metronidazole



Genital system

Condition	Recommended treatment
Gonorrhoea	Intramuscular ceftriaxone + oral azithromycin
<i>Chlamydia</i>	Doxycycline or azithromycin
Pelvic inflammatory disease	Oral ofloxacin + oral metronidazole or intramuscular ceftriaxone + oral doxycycline + oral metronidazole
Syphilis	Benzathine benzylpenicillin or doxycycline or erythromycin
Bacterial vaginosis	Oral or topical metronidazole or topical clindamycin

Gastrointestinal

Condition	Recommended treatment
<i>Clostridium difficile</i>	First episode: metronidazole Second or subsequent episode of infection: vancomycin
Campylobacter enteritis	Clarithromycin
Salmonella (non-typhoid)	Ciprofloxacin
Shigellosis	Ciprofloxacin

*a combined topical antibiotic and corticosteroid is generally used for mild/moderate cases of otitis externa

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What type of drug is Metronidazole?

Inactive

Detoxified

Extracted

Live attenuated

Metronidazole is a type of antibiotic that works by forming reactive cytotoxic metabolites inside the bacteria.

Adverse effects

- disulfiram-like reaction with alcohol

Vancomycin

Vancomycin is a glycopeptide antibiotic used in the treatment of Gram positive infections, particularly methicillin-resistant *Staphylococcus aureus* (MRSA).

Mechanism of action

- inhibits cell wall formation by binding to D-Ala-D-Ala moieties, preventing polymerization of peptidoglycans

Mechanism of resistance

- alteration to the terminal amino acid residues of the NAM/NAG-peptide subunits (normally D-alanyl-D-alanine) to which the antibiotic binds

Adverse effects

- nephrotoxicity
- ototoxicity
- thrombophlebitis
- red man syndrome; occurs on rapid infusion of vancomycin

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Sulfonamides

Sulfonamides are a class of antibiotic that work by inhibiting dihydropteroate synthetase

Examples

- co-trimoxazole
- trimethoprim

Adverse effects of co-trimoxazole include:

- Steven-Johnson syndrome

Cephalosporins

Cephalosporins are a type of β -lactam antibiotic which are bactericidal. They are less susceptible to penicillinases than penicillins.

β -lactam antibiotics work by disrupting the synthesis of bacterial cell walls, by inhibiting peptidoglycan cross-linking.

Mechanism of resistance

- Changes to penicillin-binding-proteins (PBPs), which are types of transpeptidases (enzymes produced by bacteria that cross-links peptidoglycan chains to form rigid cell walls)



Trimethoprim

Trimethoprim is an antibiotic, mainly used in the management of urinary tract infections.

Mechanism of action

- interferes with DNA synthesis by inhibiting dihydrofolate reductase

Adverse effects

- myelosuppression
- transient rise in creatinine: trimethoprim competitively inhibits the tubular secretion of creatinine resulting in a temporary increase which reverses upon stopping the drug

Next question >

Tetracyclines

Tetracyclines are a class of antibiotics which are commonly used in clinical practice.

Examples

- doxycycline
- tetracycline

Mechanism of action

- protein synthesis inhibitors
- binds to 30S subunit blocking binding of aminoacyl-tRNA

Mechanism of resistance

- increased efflux of the bacteria by plasmid-encoded transport pumps, ribosomal protection

Indications

- acne vulgaris
- Lyme disease
- *Chlamydia*

-*Mycoplasma pneumoniae*

Adverse effects

- discolouration of teeth
 - photosensitivity
-

Linezolid

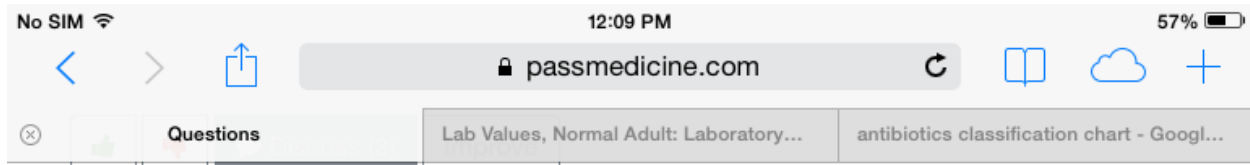
Linezolid is a type of oxazolidinone antibiotic which has been introduced in recent years. It inhibits bacterial protein synthesis by stopping formation of the 70s initiation complex and is bacteriostatic nature

Spectrum, highly active against Gram positive organisms including:

- MRSA (Methicillin-resistant *Staphylococcus aureus*)
- VRE (Vancomycin-resistant enterococcus)
- GISA (Glycopeptide Intermediate *Staphylococcus aureus*)

Adverse effects

- thrombocytopenia (reversible on stopping)
 - monoamine oxidase inhibitor: avoid tyramine containing foods
-



Next question >

Antibiotics: bactericidal vs. bacteriostatic

Bactericidal antibiotics

- penicillins
- cephalosporins
- aminoglycosides
- nitrofurantoin
- metronidazole
- quinolones
- rifampicin
- isoniazid

Bacteriostatic antibiotics

- chloramphenicol
- macrolides
- tetracyclines
- sulphonamides
- trimethoprim

Next question >

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Save my notes

The table below lists the more common respiratory pathogens:

Pathogen	Associated condition
Respiratory syncytial virus	Bronchiolitis
Parainfluenza virus	Croup
Rhinovirus	Common cold
Influenza virus	Flu
<i>Streptococcus pneumoniae</i>	The most common cause of community-acquired pneumonia
<i>Haemophilus influenzae</i>	Community-acquired pneumonia Most common cause of bronchiectasis exacerbations Acute epiglottitis
<i>Staphylococcus aureus</i>	Pneumonia, particularly following influenza
<i>Mycoplasma pneumoniae</i>	Atypical pneumonia Flu-like symptoms classically precede a dry cough. Complications include haemolytic anaemia and erythema multiforme
<i>Legionella pneumophila</i>	Atypical pneumonia Classically spread by air-conditioning systems, causes dry cough. Lymphopenia, deranged liver function tests and hyponatraemia may be seen
Pneumocystis jiroveci	Common cause of pneumonia in HIV patients. Typically patients have few chest signs and develop exertional dyspnoea
<i>Mycobacterium tuberculosis</i>	Causes tuberculosis. A wide range of presentations from asymptomatic to disseminated disease are possible. Cough, night sweats and weight loss may be seen

Pneumonia: causes

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- *Staphylococcus aureus*: commonly after the 'flu
- atypical pneumonias (e.g. Due to *Mycoplasma pneumoniae*)
- viruses

Klebsiella pneumoniae is classically in alcoholics

***Streptococcus pneumoniae* (pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

Tuberculosis: screening

The Mantoux test is the main technique used to screen for latent tuberculosis. In recent years the interferon-gamma blood test has also been introduced. It is used in a number of specific situations such as:

- the Mantoux test is positive or equivocal
- people where a tuberculin test may be falsely negative (see below)

Mantoux test

- 0.1 ml of 1:1,000 purified protein derivative (PPD) injected intradermally
- result read 2-3 days later

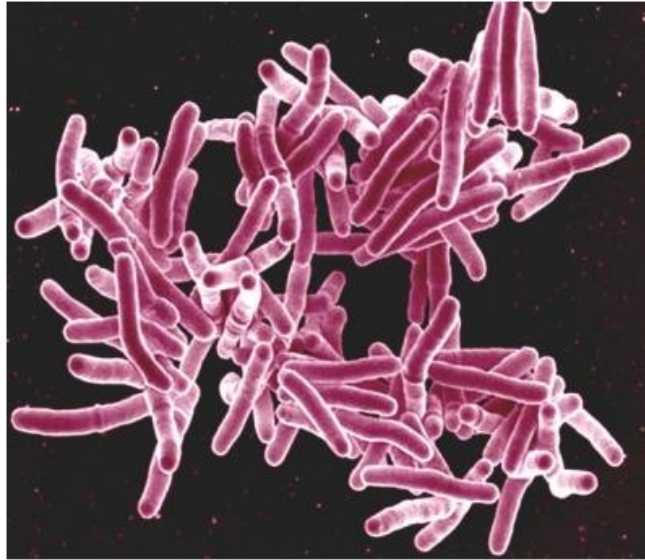
Diameter of induration	Positivity	Interpretation
< 6mm	Negative - no significant hypersensitivity to tuberculin protein	Previously unvaccinated individuals may be given the BCG
6 - 15mm	Positive - hypersensitive to tuberculin protein	Should not be given BCG. May be due to previous TB infection or BCG
> 15mm	Strongly positive - strongly hypersensitive to tuberculin protein	Suggests tuberculosis infection.

False negative tests may be caused by:

- miliary TB
- sarcoidosis
- HIV
- lymphoma
- very young age (e.g. < 6 months)

Heaf test

The Heaf test was previously used in the UK but has been since been discontinued. It involved injection of PPD equivalent to 100,000 units per ml to the skin over the flexor surface of the left forearm. It was then read 3-10 days later.



Scanning electron micrograph of *Mycobacterium tuberculosis* bacteria, which cause TB. Credit: NIAID

Next question >

Tuberculosis: drug therapy

The standard therapy for treating **active tuberculosis** is:

Initial phase - first 2 months (RIPE)

- Rifampicin
- Isoniazid
- Pyrazinamide
- Ethambutol (the 2006 NICE guidelines now recommend giving a 'fourth drug' such as ethambutol routinely - previously this was only added if drug-resistant tuberculosis was suspected)

Continuation phase - next 4 months

- Rifampicin
- Isoniazid

The treatment for **latent tuberculosis** is isoniazid alone for 6 months

Patients with **meningeal tuberculosis** are treated for a prolonged period (at least 12 months) with the addition of steroids

Directly observed therapy with a three times a week dosing regimen may be indicated in certain groups, including:

- homeless people with active tuberculosis
- patients who are likely to have poor concordance
- all prisoners with active or latent tuberculosis

Next question >

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Legionella

Legionnaire's disease is caused by the intracellular bacterium *Legionella pneumophila*. It typically colonizes water tanks and hence questions may hint at air-conditioning systems or foreign holidays. Person-to-person transmission is not seen

Features

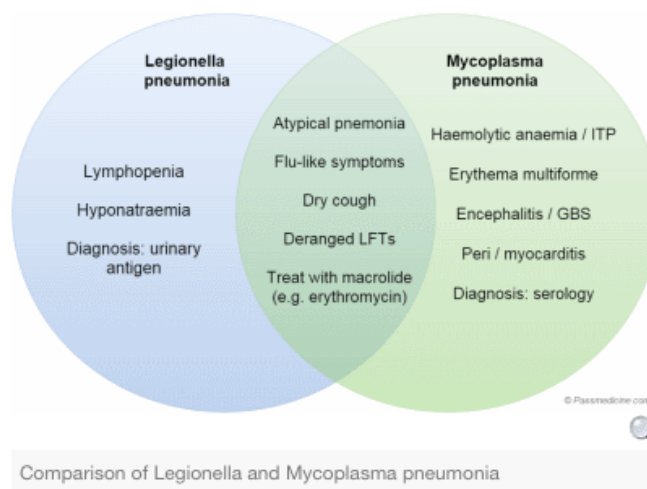
- flu-like symptoms including fever (present in > 95% of patients)
- dry cough
- relative bradycardia
- confusion
- lymphopaenia
- hyponatraemia
- deranged liver function tests
- pleural effusion: seen in around 30% of patients

Diagnosis

- urinary antigen

Management

- treat with erythromycin



Mycoplasma pneumoniae

Mycoplasma pneumoniae is a cause of atypical pneumonia which often affects younger patients. It is associated with a number of characteristic complications such as erythema multiforme and cold autoimmune haemolytic anaemia. Epidemics of *Mycoplasma pneumoniae* classically occur every 4 years. It is important to recognise atypical pneumonias as they may not respond to penicillins or cephalosporins due to it lacking a peptidoglycan cell wall.

Features

- the disease typically has a prolonged and gradual onset
- flu-like symptoms classically precede a dry cough
- bilateral consolidation on x-ray
- complications may occur as below

Complications

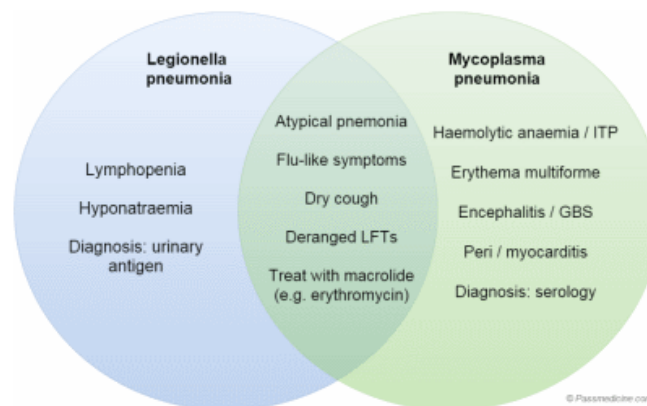
- cold agglutins (IgM) may cause an haemolytic anaemia, thrombocytopenia
- erythema multiforme, erythema nodosum
- meningoencephalitis, Guillain-Barre syndrome
- bullous myringitis: painful vesicles on the tympanic membrane
- pericarditis/myocarditis
- gastrointestinal: hepatitis, pancreatitis
- renal: acute glomerulonephritis

Investigations

- diagnosis is generally by *Mycoplasma* serology
- positive cold agglutination test

Management

- erythromycin/clarithromycin
- tetracyclines such as doxycycline are an alternative



Less relevant

Meningitis: causes

0 - 3 months

- Group B *Streptococcus* (most common cause in neonates)
- *E. coli*
- *Listeria monocytogenes*

3 months - 6 years

- *Neisseria meningitidis*
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*

6 years - 60 years

- *Neisseria meningitidis*
- *Streptococcus pneumoniae*

> 60 years

- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- *Listeria monocytogenes*

Immunosuppressed

- *Listeria monocytogenes*

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Meningococcal septicaemia: investigations

Meningococcal septicaemia is a frightening condition for patients, parents and doctors. It is associated with a high morbidity and mortality unless treated early - meningococcal disease is the leading infectious cause of death in early childhood. A high index of suspicion is therefore needed. Much of the following is based on the 2010 NICE guidelines (please see link).

Presentation of meningococcal disease:

- 15% - meningitis
- 25% - septicaemia
- 60% - a combination of meningitis and septicaemia

Investigations

- blood cultures
- blood PCR
- lumbar puncture is usually contraindicated
- full blood count and clotting to assess for disseminated intravascular coagulation

Meningitis: CSF analysis

The table below summarises the characteristic cerebrospinal fluid (CSF) findings in meningitis:

	Bacterial	Viral	Tuberculous
Appearance	Cloudy	Clear/cloudy	Slight cloudy, fibrin web
Glucose	Low (< 1/2 plasma)	60-80% of plasma glucose*	Low (< 1/2 plasma)
Protein	High (> 1 g/l)	Normal/raised	High (> 1 g/l)
White cells	10 - 5,000 polymorphs/mm ³	15 - 1,000 lymphocytes/mm ³	10 - 1,000 lymphocytes/mm ³

The Ziehl-Neelsen stain is only 20% sensitive in the detection of tuberculous meningitis and therefore PCR is sometimes used (sensitivity = 75%)

*mumps is unusual in being associated with a low glucose level in a proportion of cases. A low glucose may also be seen in herpes encephalitis



Meningitis: management

Investigations suggested by NICE

- full blood count
- CRP
- coagulation screen
- blood culture
- whole-blood PCR
- blood glucose
- blood gas

Lumbar puncture if no signs of raised intracranial pressure

Management

All patients should be transferred to hospital urgently. If patients are in a pre-hospital setting (for example a GP surgery) and meningococcal disease is suspected then intramuscular benzylpenicillin may be given, as long as this doesn't delay transit to hospital.

BNF recommendations on antibiotics

Scenario	BNF recommendation
Initial empirical therapy aged < 3 months	Intravenous cefotaxime + amoxicillin
Initial empirical therapy aged 3 months - 50 years	Intravenous cefotaxime*
Initial empirical therapy aged > 50 years	Intravenous cefotaxime + amoxicillin
Meningococcal meningitis	Intravenous benzylpenicillin or cefotaxime
Pneumococcal meningitis	Intravenous cefotaxime
Meningitis caused by <i>Haemophilus influenzae</i>	Intravenous cefotaxime
Meningitis caused by <i>Listeria</i>	Intravenous amoxicillin + gentamicin

If the patient has a history of immediate hypersensitivity reaction to penicillin or to cephalosporins the BNF recommends using chloramphenicol.

Management of contacts

- prophylaxis needs to be offered to household and close contacts of patients affected with meningococcal meningitis
- oral ciprofloxacin or rifampicin or may be used. The Health Protection Agency (HPA) guidelines now state

If the patient has a history of immediate hypersensitivity reaction to penicillin or to cephalosporins the BNF recommends using chloramphenicol.

Management of contacts

- prophylaxis needs to be offered to household and close contacts of patients affected with meningococcal meningitis
- oral ciprofloxacin or rifampicin or may be used. The Health Protection Agency (HPA) guidelines now state that whilst either may be used ciprofloxacin is the drug of choice as it is widely available and only requires one dose
- the risk is highest in the first 7 days but persists for at least 4 weeks
- meningococcal vaccination should be offered to close contacts when serotype results are available, including booster doses to those who had the vaccine in infancy
- for pneumococcal meningitis no prophylaxis is generally needed. There are however exceptions to this. If a cluster of cases of pneumococcal meningitis occur the HPA have a protocol for offering close contacts antibiotic prophylaxis. Please see the link for more details

*in the 2015 update of the *NICE Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management* the recommendation for initial empirically therapy for children > than 3 months is intravenous ceftriaxone



Meningococcal septicaemia: investigations

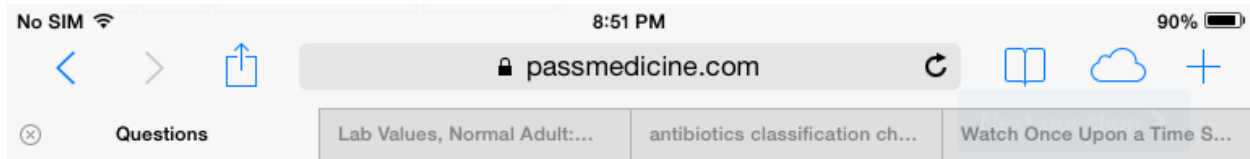
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Investigations

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- lumbar puncture is usually contraindicated
- full blood count and clotting to assess for disseminated intravascular coagulation



Sepsis

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to an infection. Sepsis is increasingly recognised as an important cause of mortality in the UK and there has been increasing efforts recently to improve the care of patients who present with sepsis.

How sepsis is classified has changed in recent years - the Surviving Sepsis Guidelines were updated in 2017.

The new guidelines recognise the following terms:

- **sepsis:** life-threatening organ dysfunction caused by a dysregulated host response to infection
- **septic shock:** a more severe form sepsis, technically defined as '*in which circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone*'*

The old category of severe sepsis is no longer used.

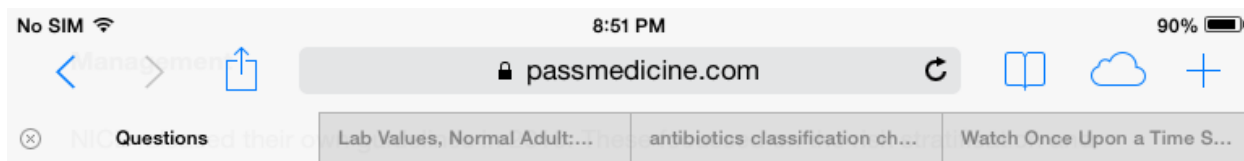
The term 'systemic inflammatory response syndrome (SIRS)' has also fallen out of favour. Adult patients outside of ICU with suspected infection are identified as being at heightened risk of mortality if they have quickSOFA (qSOFA) score meeting ≥ 2 of the following criteria: respiratory rate of 22/min or greater, altered mentation, or systolic blood pressure of 100mmHg or less

Management

NICE released their own guidelines in 2016. These focussed on the risk stratification and management of patients with suspected.

For risk stratification NICE recommend using the following criteria:

Red flag criteria	Amber flag criteria
• Responds only to voice or pain/	• Relatives concerned about mental



management of patients with suspected.

For risk stratification NICE recommend using the following criteria:

Red flag criteria	Amber flag criteria
• Responds only to voice or pain/ unresponsive • Acute confusional state • Systolic B.P ≤ 90 mmHg (or drop >40 from normal) • Heart rate > 130 per minute • Respiratory rate ≥ 25 per minute • Needs oxygen to keep SpO₂ $\geq 92\%$ • Non-blanching rash, mottled/ ashen/ cyanotic • Not passed urine in last 18 h/ UO < 0.5 ml/kg/hr • Lactate ≥ 2 mmol/l • Recent chemotherapy	• Relatives concerned about mental status • Acute deterioration in functional ability • Immunosuppressed • Trauma/ surgery/ procedure in last 6 weeks • Respiratory rate 21-24 • Systolic B.P 91-100 mmHg • Heart rate 91-130 OR new dysrhythmia • Not passed urine in last 12-18 hours • Temperature $< 36^{\circ}\text{C}$ • Clinical signs of wound, device or skin infection

Clearly the underlying cause of the patients sepsis needs to be identified and treated and the patient supported regardless of the cause or severity. If however any of the red flags are present the 'sepsis six' should be started straight away:

- 1. Administer oxygen: Aim to keep saturations $> 94\%$ (88-92% if at risk of CO₂ retention e.g. COPD)
- 2. Take blood cultures
- 3. Give broad spectrum antibiotics
- 4. Give intravenous fluid challenges: NICE recommend a bolus of 500ml crystalloid over less than 15 minutes
- 5. Measure serum lactate
- 6. Measure accurate hourly urine output

*these patients can be clinically identified by a vasopressor requirement to maintain a MAP ≥ 65 mmHg and serum lactate >2 mmol/L in the absence of hypovolemia

Necrotising fasciitis

Necrotising fasciitis is a medical emergency that is difficult to recognise in the early stages

It can be classified according to the causative organism:

- type 1 is caused by mixed anaerobes and aerobes (often occurs post-surgery in diabetics)
- type 2 is caused by *Streptococcus pyogenes*

Features

- acute onset
- painful, erythematous lesion develops
- extremely tender over infected tissue

Management

- urgent surgical referral debridement
 - intravenous antibiotics
-

Cellulitis

Cellulitis is a term used to describe an inflammation of the skin and subcutaneous tissues, typically due to infection by *Streptococcus pyogenes* or *Staphylococcus aureus*.

Features

- commonly occurs on the shins
- erythema, pain, swelling
- there may be some associated systemic upset such as fever

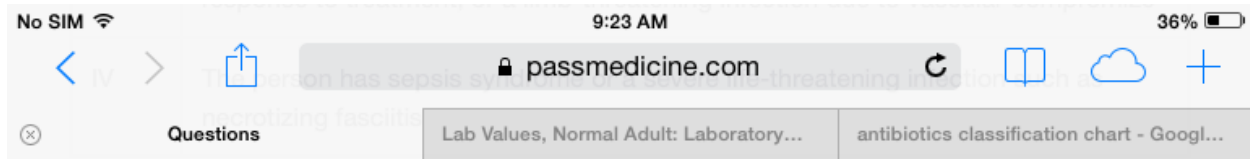
Criteria for admission

NICE Clinical Knowledge Summaries recommend we use the Eron classification to guide how we manage patients with cellulitis:

Class	Features
I	There are no signs of systemic toxicity and the person has no uncontrolled co-morbidities
II	The person is either systemically unwell or systemically well but with a co-morbidity (for example peripheral arterial disease, chronic venous insufficiency, or morbid obesity) which may complicate or delay resolution of infection
III	The person has significant systemic upset such as acute confusion, tachycardia, tachypnoea, hypotension, or unstable co-morbidities that may interfere with a response to treatment, or a limb-threatening infection due to vascular compromise
IV	The person has sepsis syndrome or a severe life-threatening infection such as necrotizing fasciitis

They recommend the following that we admit for intravenous antibiotics the following patients:

- Has Eron Class III or Class IV cellulitis.
- Has severe or rapidly deteriorating cellulitis (for example extensive areas of skin).
- Is very young (under 1 year of age) or frail



They recommend the following that we admit for intravenous antibiotics the following patients:

- Has Eron Class III or Class IV cellulitis.
- Has severe or rapidly deteriorating cellulitis (for example extensive areas of skin).
- Is very young (under 1 year of age) or frail.
- Is immunocompromized.
- Has significant lymphoedema.
- Has facial cellulitis (unless very mild) or periorbital cellulitis.

The following is recommend regarding Eron Class II cellulitis:

Admission may not be necessary if the facilities and expertise are available in the community to give intravenous antibiotics and monitor the person - check local guidelines.

Other patients can be treated with oral antibiotics.

Management

The BNF recommends flucloxacillin as first-line treatment for mild/moderate cellulitis. Clarithromycin or clindamycin is recommend in patients allergic to penicillin.

Many local protocols now suggest the use of oral clindamycin in patients who have failed to respond to flucloxacillin.

Severe cellulitis should be treated with intravenous benzylpenicillin + flucloxacillin.



Anthrax



Question

What is the

Human

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Macrop

Defect

Antibod

Anthrax is caused by *Bacillus anthracis*, a Gram positive rod. It is spread by infected carcasses. It is also known as Woolsorters' disease. *Bacillus anthracis* produces a tripartite protein toxin

- protective antigen
- oedema factor: a bacterial adenylate cyclase which increases cAMP
- lethal factor: toxic to macrophages

Features

- causes painless black eschar (cutaneous 'malignant pustule', but no pus)
- typically painless and non-tender
- may cause marked oedema
- anthrax can cause gastrointestinal bleeding

Management

- the current Health Protection Agency advice for the initial management of cutaneous anthrax is ciprofloxacin
- further treatment is based on microbiological investigations and expert advice

Staphylococcal toxic shock syndrome



A 6-year-
character

Staphylococcal toxic shock syndrome describes a severe systemic reaction to staphylococcal exotoxins. It came to prominence in the early 1980's following a series of cases related to infected tampons

Adenov

Epstein

Rubella

Coxsac

Parvov

Rotavir

Centers for Disease Control and Prevention diagnostic criteria

- fever: temperature $> 38.9^{\circ}\text{C}$
- hypotension: systolic blood pressure < 90 mmHg
- diffuse erythematous rash
- desquamation of rash, especially of the palms and soles
- involvement of three or more organ systems: e.g. gastrointestinal (diarrhoea and vomiting), mucous membrane erythema, renal failure, hepatitis, thrombocytopenia, CNS involvement (e.g. confusion)



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palms

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Streptococci



Hepatitis

Osteop

Pancre

Warm a

Tumour

Cryoglo

Hypoga

Streptococci are gram-positive cocci. They may be divided into alpha and beta haemolytic types

Alpha haemolytic streptococci (partial haemolysis)

The most important alpha haemolytic *Streptococcus* is *Streptococcus pneumoniae* (pneumococcus). Pneumococcus is a common cause of pneumonia, meningitis and otitis media. Another clinical example is *Streptococcus viridans*

Beta haemolytic streptococci (complete haemolysis)

These can be subdivided into groups A-H. Only groups A, B & D are important in humans.

Group A

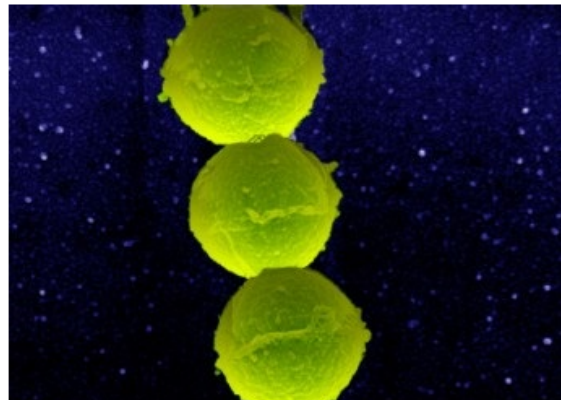
- most important organism is *Streptococcus pyogenes*
- responsible for erysipelas, impetigo, cellulitis, type 2 necrotizing fasciitis and pharyngitis/tonsillitis
- immunological reactions can cause rheumatic fever or post-streptococcal glomerulonephritis
- erythrogenic toxins cause scarlet fever

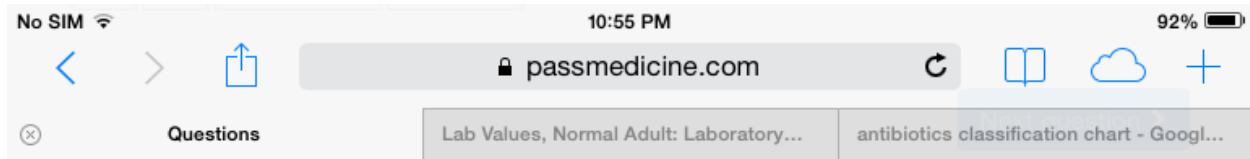
Group B

- *Streptococcus agalactiae* may lead to neonatal meningitis and septicaemia

Group D

- *Enterococcus*





MRSA

Methicillin-resistant *Staphylococcus aureus* (MRSA) was one of the first organisms which highlighted the dangers of hospital-acquired infections.

Who should be screened for MRSA?

- all patients awaiting elective admissions (exceptions include day patients having terminations of pregnancy and ophthalmic surgery. Patients admitted to mental health trusts are also excluded)
- from 2011 all emergency admissions will be screened

How should a patient be screened for MRSA?

- nasal swab and skin lesions or wounds
- the swab should be wiped around the inside rim of a patient's nose for 5 seconds
- the microbiology form must be labelled 'MRSA screen'

Suppression of MRSA from a carrier once identified

- nose: mupirocin 2% in white soft paraffin, tds for 5 days
- skin: chlorhexidine gluconate, od for 5 days. Apply all over but particularly to the axilla, groin and perineum

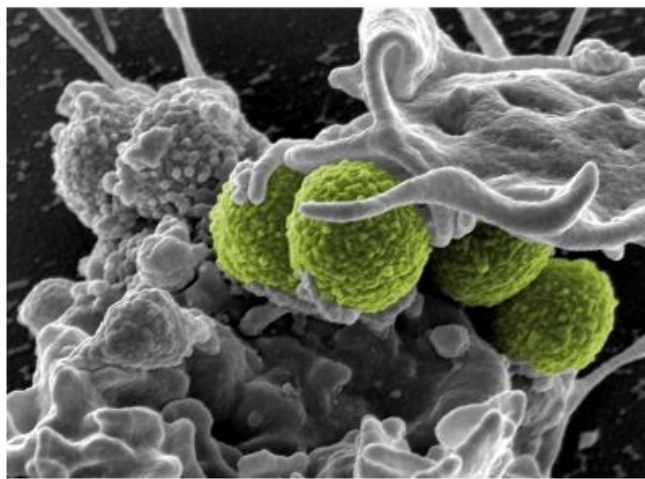
The following antibiotics are commonly used in the treatment of MRSA infections:

- vancomycin
- teicoplanin
- linezolid

Some strains may be sensitive to the antibiotics listed below but they should not generally be used alone because resistance may develop:

- rifampicin
- macrolides
- tetracyclines
- aminoglycosides
- clindamycin

Relatively new antibiotics such as linezolid, quinupristin/dalfopristin combinations and tigecycline have activity against MRSA but should be reserved for resistant cases



Interaction of MRSA (green bacteria) with a human white cell. The bacteria shown is strain MRSA252, a leading cause of hospital-associated infections in the United States and United Kingdom. Credit: NIAID



Syphilis



Question

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*. Infection is characterised by primary, secondary and tertiary stages. The incubation period is between 9-90 days

At what stage

Primary features

- chancre - painless ulcer at the site of sexual contact
- local non-tender lymphadenopathy
- often not seen in women (the lesion may be on the cervix)

CD4 200

CD4 100

CD4 500

CD4 < 350

Secondary features - occurs 6-10 weeks after primary infection

- systemic symptoms: fevers, lymphadenopathy
- rash on trunk, palms and soles
- buccal 'snail track' ulcers (30%)
- condylomata lata

258 facts

Score for

3 in a row

Key facts



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Classical palm lesions of secondary syphilis

Hutchinson

Oesophagitis

Cytomegalovirus

Aspergillus

tion

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Syphilis: investigation

Treponema pallidum is a very sensitive organism and cannot be grown on artificial media. The diagnosis is therefore usually based on clinical features, serology and microscopic examination of infected tissue

Serological tests can be divided into

- cardiolipin tests (not treponeme specific)
- treponemal specific antibody tests

Cardiolipin tests

- syphilis infection leads to the production of non-specific antibodies that react to cardiolipin
- examples include VDRL (Venereal Disease Research Laboratory) & RPR (rapid plasma reagin)
- insensitive in late syphilis
- becomes negative after treatment

Treponemal specific antibody tests

- example: TPHA (*Treponema pallidum* HaemAgglutination test)
- remains positive after treatment

Causes of false positive cardiolipin tests

- pregnancy
- SLE, anti-phospholipid syndrome
- TB
- leprosy
- malaria
- HIV



Syphilis: management

Management

- benzylpenicillin
- alternatives: doxycycline
- the Jarisch-Herxheimer reaction is sometimes seen following treatment. Fever, rash, tachycardia after first dose of antibiotic. It is thought to be due to the release of endotoxins following bacterial death and typically occurs within a few hours of treatment.

Cat scratch disease

Cat scratch disease is generally caused by the Gram negative rod *Bartonella henselae*

Features

- fever
- history of a cat scratch
- regional lymphadenopathy
- headache, malaise

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Questions Lab Values, Normal Adult: Laboratory... antibiotics classification chart - Googl...

Discuss (3) Improve

Next question >

Leptospirosis

Also known as Weil's disease*, leptospirosis is commonly seen in questions referring to sewage workers, farmers, vets or people who work in abattoir. It is caused by the spirochaete *Leptospira interrogans* (serogroup L icterohaemorrhagiae), classically being spread by contact with infected rat urine. Weil's disease should always be considered in high-risk patients with hepatorenal failure

Features

- fever
- flu-like symptoms
- renal failure (seen in 50% of patients)
- jaundice
- subconjunctival haemorrhage
- headache, may herald the onset of meningitis

Management

- high-dose benzylpenicillin or doxycycline

*the term Weil's disease is sometimes reserved for the most severe 10% of cases that are associated with jaundice

Next question >

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Next question >

Leprosy

Leprosy is a granulomatous disease primarily affecting the peripheral nerves and skin. It is caused by *Mycobacterium leprae*.

Features

- patches of hypopigmented skin typically affecting the buttocks, face, and extensor surfaces of limbs
- sensory loss

The degree of cell mediated immunity determines the type of leprosy a patient will develop.

Low degree of cell mediated immunity → lepromatous leprosy ('multibacillary')

- extensive skin involvement
- symmetrical nerve involvement

High degree of cell mediated immunity → tuberculoid leprosy ('paucibacillary')

- limited skin disease
- asymmetric nerve involvement

Management

- WHO-recommended triple therapy: rifampicin, dapsone and clofazimine

Next question >

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antibiotics classification chart - Googl...

Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Stereotypical histories

Infection	Typical presentation
<i>Escherichia coli</i>	Common amongst travellers Watery stools Abdominal cramps and nausea
Giardiasis	Prolonged, non-bloody diarrhoea
Cholera	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
<i>Shigella</i>	Bloody diarrhoea Vomiting and abdominal pain
<i>Staphylococcus aureus</i>	Severe vomiting Short incubation period
<i>Campylobacter</i>	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody Complications include Guillain-Barre syndrome
<i>Bacillus cereus</i>	Two types of illness are seen • vomiting within 6 hours, stereotypically due to rice • diarrhoeal illness occurring after 6 hours
Amoebiasis	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

Incubation period

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Stereotypical histories

Infection	Typical presentation
<i>Escherichia coli</i>	Common amongst travellers Watery stools Abdominal cramps and nausea
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Amoebiasis	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus**
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

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Question 17

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Amantadine may cause ataxia

Notes (1/1)

Cryptosporidiosis

Cryptosporidiosis is the commonest protozoal cause of diarrhoea in the UK. Two species, *Cryptosporidium hominis* and *Cryptosporidium parvum* account for the majority cases.

Cryptosporidiosis is more common in immunocompromised patients (e.g. HIV) and young children.

Features

- watery diarrhoea
- abdominal cramps
- fever
- in immunocompromised patients the entire gastrointestinal tract may be affected resulting in complications such as sclerosing cholangitis and pancreatitis

Diagnosis

- stool: modified Ziehl-Neelsen stain (acid-fast stain) of the stool may reveal the characteristic red cysts of *Cryptosporidium*

Management

- is largely supportive
- nitazoxanide is licensed in the US for immunocompetent patients

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Close

Clostridia

Clostridia are gram-positive, obligate anaerobic bacilli.

C. perfringens

- produces α -toxin, a lecithinase, which causes gas gangrene (myonecrosis) and haemolysis
- features include tender, oedematous skin with haemorrhagic blebs and bullae. Crepitus may present on palpation

C. botulinum

- typically seen in canned foods and honey
- prevents acetylcholine (ACh) release leading to flaccid paralysis

C. difficile

- causes pseudomembranous colitis, typically seen after the use of broad-spectrum antibiotics
- produces both an exotoxin and a cytotoxin

C. tetani

- produces an exotoxin (tetanospasmin) that prevents the release of glycine from Renshaw cells in the spinal cord causing a spastic paralysis

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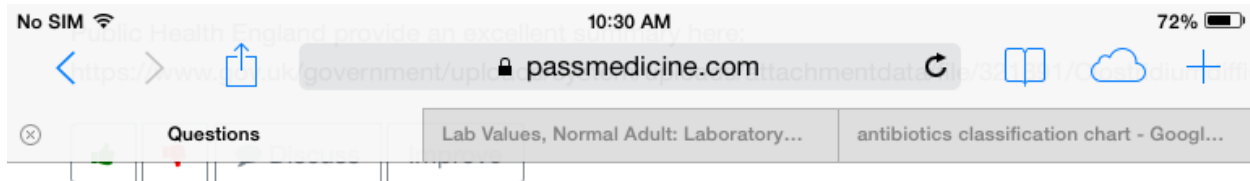
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Score for this session: **76.2%**

Key facts from this session are shown below (score/attempts), click on the fact for background information



Next question >

Clostridium difficile

Clostridium difficile is a Gram positive rod often encountered in hospital practice. In the UK it can be found in 3% of normal adults and up to 66% of babies. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis.

Risk factors

- Broad spectrum antibiotics
- Use of PPI and H₂ receptor antagonists
- Contacted with persons infected with *C. difficile*

Features

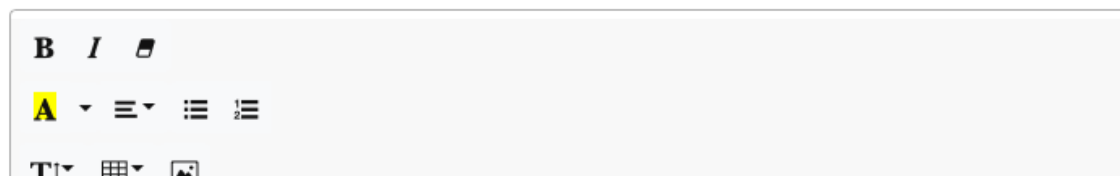
- Diarrhoea
- Abdominal pain
- A raised white blood cell count is characteristic
- If severe, toxic megacolon may develop

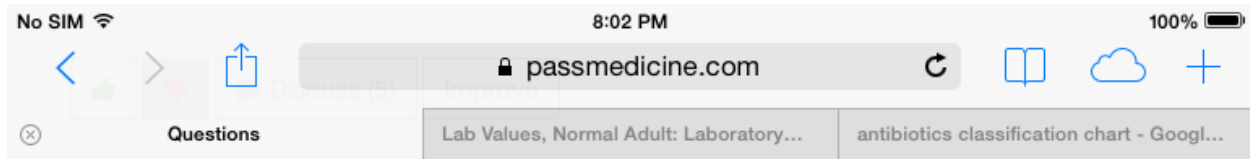
Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

Management

- First-line therapy is oral metronidazole for 10-14 days
- If severe, or not responding to metronidazole, then oral vancomycin may be used
- Patients who do not respond to vancomycin may respond to oral fidaxomicin
- Patients with severe and unremitting colitis should be considered for colectomy

Next question >





Salmonella

The *Salmonella* group contains many members, most of which cause diarrhoeal diseases. They are aerobic, Gram negative rods which are not normally present as commensals in the gut.

Typhoid and paratyphoid are caused by *Salmonella typhi* and *Salmonella paratyphi* (types A, B & C) respectively. They are often termed enteric fevers, producing systemic symptoms such as headache, fever, arthralgia

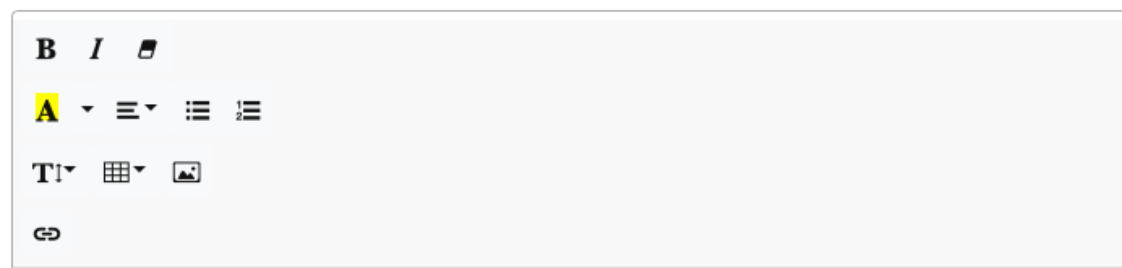
Features

- initially systemic upset as above
- relative bradycardia
- abdominal pain, distension
- constipation: although *Salmonella* is a recognised cause of diarrhoea, constipation is more common in typhoid
- rose spots: present on the trunk in 40% of patients, and are more common in paratyphoid

Possible complications include

- osteomyelitis (especially in sickle cell disease where *Salmonella* is one of the most common pathogens)
- GI bleed/perforation
- meningitis
- cholecystitis
- chronic carriage (1%, more likely if adult females)

Next question >



Giardiasis

Giardiasis is caused by the flagellate protozoan *Giardia lamblia*. It is spread by the faeco-oral route

Features

- often asymptomatic
- lethargy, bloating, abdominal pain
- non-bloody diarrhoea
- chronic diarrhoea, malabsorption and lactose intolerance can occur
- stool microscopy for trophozoite and cysts are classically negative, therefore duodenal fluid aspirates or 'string tests' (fluid absorbed onto swallowed string) are sometimes needed

Treatment is with metronidazole

Cholera

Overview

- caused by *Vibrio cholerae* - Gram negative bacteria

Features

- profuse 'rice water' diarrhoea
- dehydration
- hypoglycaemia

Management

- oral rehydration therapy
 - antibiotics: doxycycline, ciprofloxacin
-

Diphtheria

Diphtheria is caused by the Gram positive bacterium *Corynebacterium diphtheriae*

Pathophysiology

- releases an exotoxin encoded by a β -prophage
- exotoxin inhibits protein synthesis by catalyzing ADP-ribosylation of elongation factor EF-2

Diphtheria toxin commonly causes a 'diphtheric membrane' on tonsils caused by necrotic mucosal cells. Systemic distribution may produce necrosis of myocardial, neural and renal tissue

Possible presentations

- recent visitors to Eastern Europe/Russia/Asia
- sore throat with a 'diphtheric membrane' - see above
- bulky cervical lymphadenopathy
- neuritis e.g. cranial nerves
- heart block





Next question >

Brucellosis

Brucellosis is a zoonosis more common in the Middle East and in farmers. Four major species cause infection in humans: *B melitensis* (sheep), *B abortus* (cattle), *B canis* and *B suis* (pigs). Brucellosis has an incubation period 2 - 6 weeks

Features

- non-specific: fever, malaise
- hepatosplenomegaly
- sacroilitis: spinal tenderness may be seen
- complications: osteomyelitis, infective endocarditis, meningoencephalitis, orchitis
- leukopenia often seen

Diagnosis

- the Rose Bengal plate test can be used for screening but other tests are required to confirm the diagnosis
- Brucella serology is the best test for diagnosis
- blood and bone marrow cultures may be suitable in certain patients, but these tests are often negative

Management

- doxycycline and streptomycin

Next question >





Next question >

Tetanus

Tetanus is caused by the tetanospasmin exotoxin released from *Clostridium tetani*. Tetanus spores are present in soil and may be introduced into the body from a wound, which is often unnoticed. Tetanospasmin prevents release of GABA

Features

- prodrome fever, lethargy, headache
- trismus (lockjaw)
- risus sardonicus
- opisthotonus (arched back, hyperextended neck)
- spasms (e.g. dysphagia)

Management

- supportive therapy including ventilatory support and muscle relaxants
- intramuscular human tetanus immunoglobulin for high-risk wounds (e.g. compound fractures, delayed surgical intervention, significant degree of devitalised tissue)
- metronidazole is now preferred to benzylpenicillin as the antibiotic of choice

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Questions Lab Values, Normal Adult: Laboratory... antibiotics classification chart - Googl...

Discuss Improve

Next question >

Botulism

Clostridium botulinum

- gram positive anaerobic bacillus
- 7 serotypes A-G
- produces botulinum toxin, a neurotoxin which irreversibly blocks the release of acetylcholine
- may result from eating contaminated food (e.g. tinned)
- neurotoxin often affects bulbar muscles and autonomic nervous system

Features

- patient usually fully conscious with no sensory disturbance
- flaccid paralysis
- diplopia
- ataxia
- bulbar palsy

Treatment with antitoxin is only effective if given early - once toxin has bound its actions cannot be reversed

Therapeutic uses of botulinum toxin

- strabismus
- dystonias: torticollis, blepharospasm
- hyperhidrosis
- cosmetic: Botox: serotype A of botulinum toxin used

Next question >

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Lyme disease



Question

Lyme disease is caused by the spirochaete *Borrelia burgdorferi* and is spread by ticks

Tables do

Primary

Congenital

Tertiary

Secondary

Features

- early: erythema chronicum migrans + systemic features (fever, arthralgia)
- CVS: heart block, myocarditis
- neuro: cranial nerve palsies, meningitis

Investigation

- serology: antibodies to *Borrelia burgdorferi*. These can take 3-8 weeks before they are detectable

Management

- doxycycline if early disease. Amoxicillin is an alternative if doxycycline is contraindicated (e.g. pregnancy)
- ceftriaxone if disseminated disease
- Jarisch-Herxheimer reaction is sometimes seen after initiating therapy: fever, rash, tachycardia after first dose of antibiotic (more commonly seen in syphilis, another spirochaetal disease)

241 facts

Score for

Antiviral agents

Drug	Mechanism of action	Indications	Adverse effects/toxicity
Aciclovir	Guanosine analog, phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase	HSV, VZV	Crystalline nephropathy
Ganciclovir	Guanosine analog, phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase	CMV	Myelosuppression/agranulocytosis
Ribavirin	Guanosine analog which inhibits inosine monophosphate (IMP) dehydrogenase, interferes with the capping of viral mRNA	Chronic hepatitis C, RSV	Haemolytic anaemia
Amantadine	Inhibits uncoating (M2 protein) of virus in cell. Also releases dopamine from nerve endings	Influenza, Parkinson's disease	Confusion, ataxia, slurred speech
Oseltamivir	Inhibits neuraminidase	Influenza	
Foscarnet	Pyrophosphate analog which inhibits viral DNA polymerase	CMV, HSV if not responding to aciclovir	Nephrotoxicity, hypocalcaemia, hypomagnasaemia, seizures
Interferon-α	Human glycoproteins which inhibit synthesis of mRNA	Chronic hepatitis B & C, hairy cell leukaemia	Flu-like symptoms, anorexia, myelosuppression
Cidofovir	Acyclic nucleoside phosphonate, and is therefore independent of phosphorylation by viral enzymes (compare and contrast with aciclovir/ganciclovir)	CMV retinitis in HIV	Nephrotoxicity

Anti-retroviral agent used in HIV

Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine

Protease inhibitors (PI)

- inhibits a protease needed to make the virus able to survive outside the cell
- examples: indinavir, nelfinavir, ritonavir, saquinavir

Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz



Pass

RNA viruses

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Family	Structure	Envelope	Capsid Symmetry	Examples
Reoviridae	Double-stranded, linear	Naked	Icosahedral	Reovirus, Rotavirus
Picornaviridae	Single-stranded +, linear	Naked	Icosahedral	Enterovirus, Rhinovirus, Poliovirus, Coxsackie
Caliciviridae	Single-stranded +, linear	Naked	Icosahedral	Norwalk virus
Togaviridae	Single-stranded +, linear	Enveloped	Icosahedral	Rubella virus
Arenaviridae	Single-stranded -, circular	Enveloped	Helical	Lymphocytic choriomeningitis virus
Flaviviridae	Single-stranded +, linear	Enveloped	Icosahedral	Dengue virus, Hepatitis C virus, Yellow fever virus
Orthomyxoviridae	Single-stranded -, linear	Enveloped	Helical	Influenzavirus A, Influenzavirus B, Influenzavirus C,
Paramyxoviridae	Single-stranded -, linear	Enveloped	Helical	Measles virus, Mumps virus, Respiratory syncytial virus
Bunyaviridae	Single-stranded -, circular	Enveloped	Helical	California encephalitis virus, Hantavirus

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Orthomyxoviridae	Single-stranded -, linear	Enveloped	Helical	Influenzavirus A, Influenzavirus B, Influenzavirus C,
Paramyxoviridae	Single-stranded -, linear	Enveloped	Helical	Measles virus, Mumps virus, Respiratory syncytial virus
Bunyaviridae	Single-stranded -, circular	Enveloped	Helical	California encephalitis virus, Hantavirus
Rhabdoviridae	Single-stranded -, linear	Enveloped	Helical	Rabies virus
Filoviridae	Single-stranded -, linear	Enveloped	Helical	Ebola virus, Marburg virus
Coronaviridae	Single-stranded +, linear	Enveloped	Helical	Corona virus
Hepeviridae	Single-stranded +, linear	Naked	Icosahedral	Hepatitis E virus

RNA viruses memory aids:

- Reoviridae are the only double-stranded RNA viruses
- 'CALL PICO and FLAVA. There's a RETRO TOGA party with lots of CORONAs'

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Lab Values, Normal Adult: Laboratory...

antibiotics classification chart - Googl...

🔊 Less relevant ➤

DNA viruses

Family	Structure	Envelope	Examples/importance
Herpesviruses	Double-stranded, linear	Enveloped	Herpes simplex virus, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus
Hepadnavirus	Double-stranded, circular	Enveloped	Hepatitis B virus
Adenovirus	Double-stranded, linear	Naked	Common cold, conjunctivitis
Parvovirus	Single-stranded , linear	Naked	Parvovirus B19
Papillomavirus	Double-stranded, circular	Naked	HPV
Poxvirus	Double-stranded, linear	Enveloped	Smallpox, molluscum contagiosum
Polyomavirus	Double-stranded, circular	Naked	JC virus (progressive multifocal leukoencephalopathy)

Parvovirus is the only DNA virus that is not double-stranded

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Cytomegalovirus



Cytomegalovirus (CMV) is one of the herpes viruses. It is thought that around 50% of people have been exposed to the CMV virus although it only usually causes disease in the immunocompromised, for example people with HIV or those on immunosuppressants following organ transplantation.

Pathophysiology

- infected cells have a 'Owl's eye' appearance due to intranuclear inclusion bodies

Patterns of disease

Congenital CMV infection

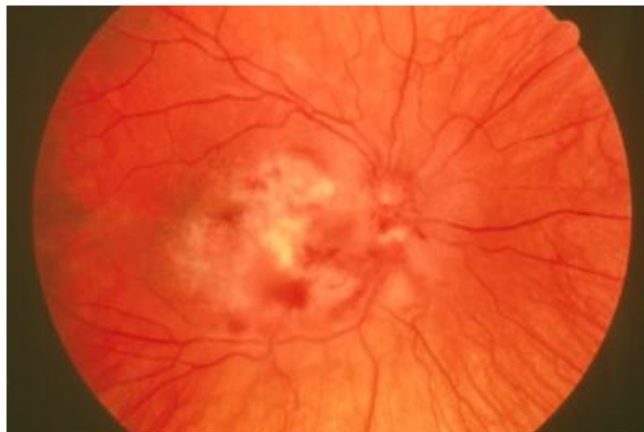
- features include growth retardation, pinpoint petechial 'blueberry muffin' skin lesions, microcephaly, sensorineural deafness, encephalitis (seizures) and hepatosplenomegaly

CMV mononucleosis

- infectious mononucleosis-like illness
- may develop in immunocompetent individuals

CMV retinitis

- common in HIV patients with a low CD4 count (< 50)
- presents with visual impairment e.g. 'blurred vision'. Fundoscopy shows retinal haemorrhages and necrosis, often called 'pizza' retina
- IV ganciclovir is the treatment of choice



Hepatitis A

Hepatitis A is typically a benign, self-limiting disease, with a serious outcome being very rare.

Overview

- incubation period: 2-4 weeks
- RNA picornavirus
- transmission is by faecal-oral spread, often in institutions
- doesn't cause chronic disease

Features

- flu-like prodrome
- jaundice, hepatosplenomegaly

Complications

- complications are rare and there is no increased risk of hepatocellular cancer

Immunisation

- an effective vaccine is available
- after the initial dose a booster dose should be given 6-12 months later

Who should be vaccinated? (Based on the Green book guidelines)

- people travelling to or going to reside in areas of high or intermediate prevalence, if aged > 1 year old
- people with chronic liver disease
- patients with haemophilia
- men who have sex with men
- injecting drug users
- individuals at occupational risk: laboratory worker; staff of large residential institutions; sewage workers; people who work with primates
- people infected with HIV

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Back to top

Hepatitis B

Hepatitis B is a double-stranded DNA hepadnavirus and is spread through exposure to infected blood or body fluids, including vertical transmission from mother to child. The incubation period is 6-20 weeks.

The features of hepatitis B include fever, jaundice and elevated liver transaminases.

Complications of hepatitis B infection

- chronic hepatitis (5-10%)
- fulminant liver failure (1%)
- hepatocellular carcinoma
- glomerulonephritis
- polyarteritis nodosa
- cryoglobulinaemia

Immunisation against hepatitis B (please see the Greenbook link for more details)

- children born in the UK are now vaccinated as part of the routine immunisation schedule. This is given at 2, 3 and 4 months of age
 - at risk groups who should be vaccinated include: healthcare workers, intravenous drug users, sex workers, close family contacts of an individual with hepatitis B, individuals receiving blood transfusions regularly, chronic kidney disease patients who may soon require renal replacement therapy, prisoners, chronic liver disease patients
 - contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology
 - around 10-15% of adults fail to respond or respond poorly to 3 doses of the vaccine. Risk factors include age over 40 years, obesity, smoking, alcohol excess and immunosuppression
 - testing for anti-HBs is only recommended for those at risk of occupational exposure (i.e. Healthcare workers) and patients with chronic kidney disease. In these patients anti-HBs levels should be checked 1-4 months after primary immunisation
 - the table below shows how to interpret anti-HBs levels:
-

Anti-HBs level (mIU/ml)	Response
> 100	Indicates adequate response, no further testing required. Should still receive booster at 5 years
10 - 100	Suboptimal response - one additional vaccine dose should be given. If immunocompetent no further testing is required
< 10	Non-responder. Test for current or past infection. Give further vaccine course (i.e. 3 doses again) with testing following. If still fails to respond then HBIG would be required for protection if exposed to the virus

Management of hepatitis B

- pegylated interferon-alpha used to be the only treatment available. It reduces viral replication in up to 30% of chronic carriers. A better response is predicted by being female, < 50 years old, low HBV DNA levels, non-Asian, HIV negative, high degree of inflammation on liver biopsy
- whilst NICE still advocate the use of pegylated interferon first-line other antiviral medications are increasingly used with an aim to suppress viral replication (not in a dissimilar way to treating HIV patients)
- examples include tenofovir and entecavir

Question

A 20-year-old male is brought to the emergency department with symptoms of acute hepatitis. He has no known risk factors for liver disease.

Legionella

Klebsiella

Haemophilus

Mycoplasma

Pneumococcus

Staphylococcus

197 factors

Score for

Key factors

Hepatitis

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Pathophysiology

- hepatitis C is a RNA flavivirus
- incubation period: 6-9 weeks

Transmission

- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%. The risk is higher if there is coexistent HIV
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

After exposure to the hepatitis C virus only around 30% of patients will develop features such as:

- a transient rise in serum aminotransferases / jaundice
- fatigue
- arthralgia

Investigations

- HCV RNA is the investigation of choice to diagnose acute infection
- whilst patients will eventually develop anti-HCV antibodies it should be remembered that patients who spontaneously clear the virus will continue to have anti-HCV antibodies

Outcome

- around 15-45% of patients will clear the virus after an acute infection (depending on their age and underlying health) and hence the majority (55-85%) will develop chronic hepatitis C

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Chronic hepatitis C

Question

Chronic hepatitis C may be defined as the persistence of HCV RNA in the blood for 6 months.

A 20-year-old male patient is brought to the clinic for examination.

Legionella

Klebsiella

Haemophilus

Mycoplasma

Pneumococcus

Staphylococcus

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Score for

Key fact

Hepatitis

Potential complications of chronic hepatitis C

- rheumatological problems: arthralgia, arthritis
- eye problems: Sjogren's syndrome
- cirrhosis (5-20% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia: typically type II (mixed monoclonal and polyclonal)
- porphyria cutanea tarda (PCT): it is increasingly recognised that PCT may develop in patients with hepatitis C, especially if there are other factors such as alcohol abuse
- membranoproliferative glomerulonephritis

Management of chronic infection

- treatment depends on the viral genotype - this should be tested prior to treatment
- the management of hepatitis C has advanced rapidly in recent years resulting in clearance rates of around 95%. Interferon based treatments are no longer recommended
- the aim of treatment is sustained virological response (SVR), defined as undetectable serum HCV RNA six months after the end of therapy
- currently a combination of protease inhibitors (e.g. daclatasvir + sofosbuvir or sofosbuvir + simeprevir) with or without ribavirin are used

Complications of treatment

- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia



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Overview

- RNA hepevirus
- spread by the faecal-oral route
- incubation period: 3-8 weeks
- common in Central and South-East Asia, North and West Africa, and in Mexico
- causes a similar disease to hepatitis A, but carries a significant mortality (about 20%) during pregnancy
- does not cause chronic disease or an increased risk of hepatocellular cancer
- a vaccine is currently in development*, but is not yet in widespread use

*New England Journal of Medicine 356:895, 2007

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HIV: immunisation

The Department of Health 'Greenbook' on immunisation defers to the British HIV Association for guidelines relating to immunisation of HIV-infected adults

Vaccines that can be used in all HIV-infected adults	Vaccines that can be used if CD4 > 200	Contraindicated in HIV-infected adults
Hepatitis A Hepatitis B <i>Haemophilus influenzae</i> B (Hib) Influenza-parenteral Japanese encephalitis Meningococcus-MenC Meningococcus-ACWY I Pneumococcus-PPV23 Poliomyelitis-parenteral (IPV) Rabies Tetanus-Diphtheria (Td)	Measles, Mumps, Rubella (MMR) Varicella Yellow Fever	Cholera CVD103-HgR Influenza-intranasal Poliomyelitis-oral (OPV) Tuberculosis (BCG)

HIV: seroconversion

HIV seroconversion is symptomatic in 60-80% of patients and typically presents as a glandular fever type illness. Increased symptomatic severity is associated with poorer long term prognosis. It typically occurs 3-12 weeks after infection

Features

- sore throat
- lymphadenopathy
- malaise, myalgia, arthralgia
- diarrhoea
- maculopapular rash
- mouth ulcers
- rarely meningoencephalitis

Diagnosis

- antibodies to HIV may not be present
- HIV PCR and p24 antigen tests can confirm diagnosis



Questions

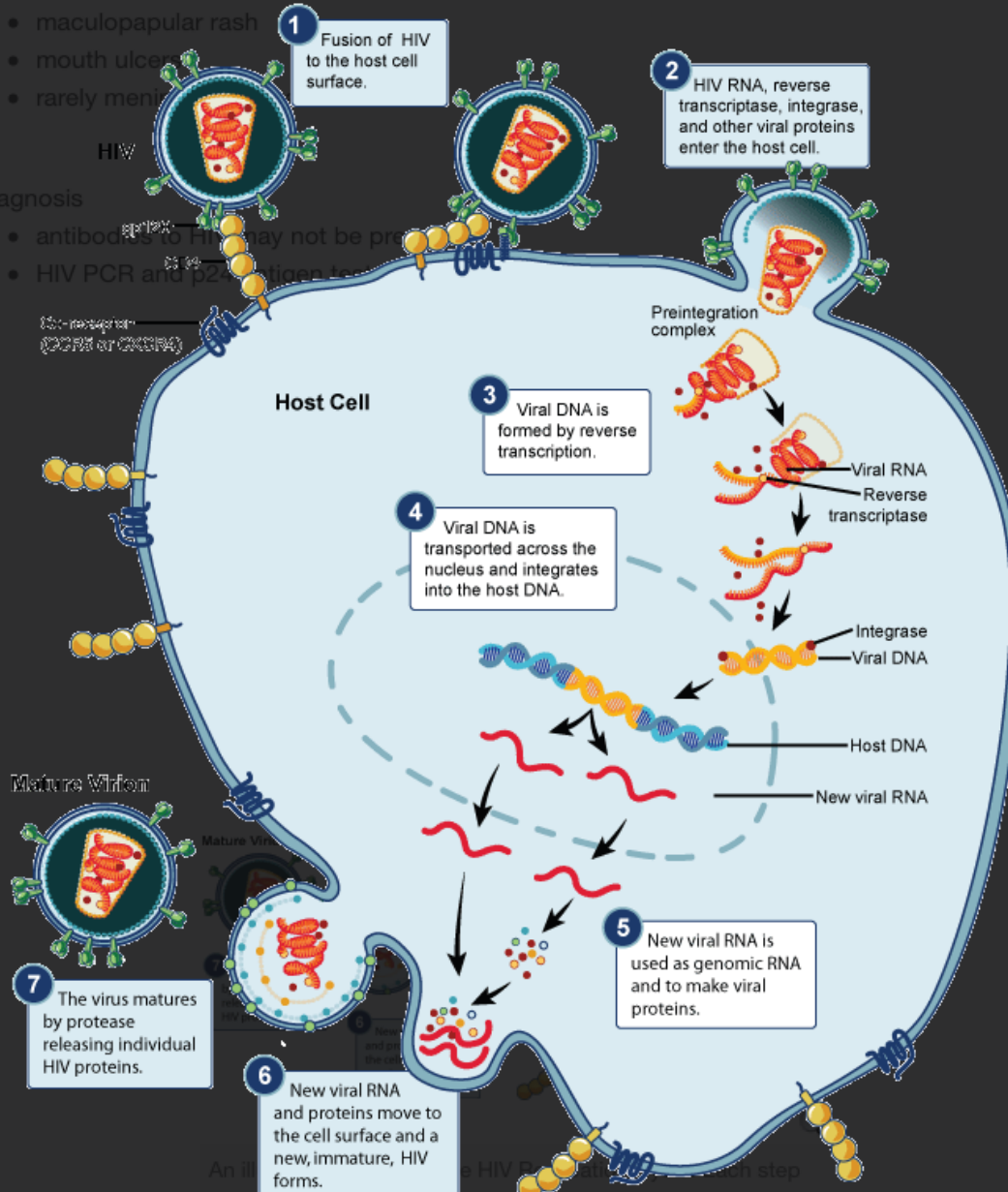
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antibiotics classification chart - Googl...

- lymphadenopathy
- malaise, myalgia, arthralgia
- diarrhoea
- maculopapular rash
- mouth ulcers
- rarely meningitis

Diagnosis

- antibodies to HIV may not be present in the first 3-6 weeks
- HIV PCR and p24 antigen test



An illustration of the HIV replication cycle. Each step of the cycle is numbered and concisely described. Credit: NIAID

Next question >



HIV: Mycobacterium avium complex

Mycobacterium avium complex (MAC) is an atypical mycobacterial infection seen in HIV patients. It is caused by both Mycobacterium avium and Mycobacterium intracellulare, and is often referred to as Mycobacterium avium-intracellulare (MAI). Over 95% of MAC infections in patients with HIV are caused by Mycobacterium avium. MAC is generally seen when the CD4 count is less than 50 cells/mm³

Features

- fever, sweats
- abdominal: pain, diarrhoea
- lung: dyspnoea, cough
- anaemia
- lymphadenopathy
- hepatomegaly/deranged LFTs

Diagnosis

- blood cultures
- bone marrow aspirate

Prophylaxis

- clarithromycin or azithromycin when CD4 is less than 100 cells/mm³

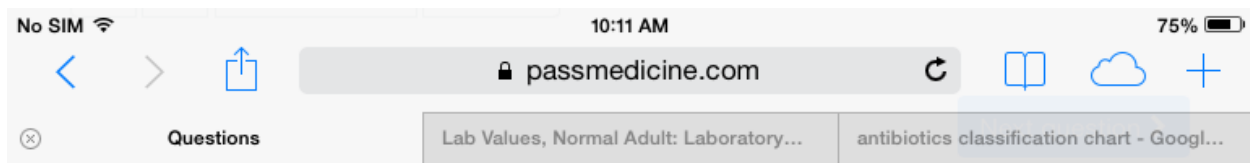
Management

- rifampicin + ethambutol + clarithromycin

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HIV and pregnancy

With the increased incidence of HIV infection amongst the heterosexual population there are an increasing number of HIV positive women giving birth in the UK. In London the incidence may be as high as 0.4% of pregnant women. The aim of treating HIV positive women during pregnancy is to minimise harm to both the mother and fetus, and to reduce the chance of vertical transmission.

Guidelines regularly change on this subject and most recent guidelines can be found using the links provided.

Factors which reduce vertical transmission (from 25-30% to 2%)

- maternal antiretroviral therapy
- mode of delivery (caesarean section)
- neonatal antiretroviral therapy
- infant feeding (bottle feeding)

Screening

- NICE guidelines recommend offering HIV screening to all pregnant women

Antiretroviral therapy

- all pregnant women should be offered antiretroviral therapy regardless of whether they were taking it previously

Mode of delivery

- vaginal delivery is recommended if viral load is less than 50 copies/ml at 36 weeks, otherwise caesarian section is recommended
- a zidovudine infusion should be started four hours before beginning the caesarean section

Neonatal antiretroviral therapy

- zidovudine is usually administered orally to the neonate if maternal viral load is <50 copies/ml. Otherwise triple ART should be used. Therapy should be continued for 4-6 weeks.

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Neonatal antiretroviral therapy

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Infant feeding

- in the UK all women should be advised not to breast feed

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HIV: Cytomegalovirus retinitis



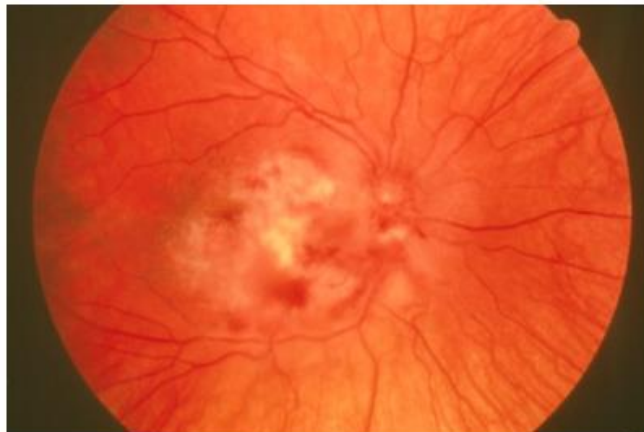
Cytomegalovirus (CMV) retinitis is common, affecting 30-40% of patients who have a CD4 count < 50 . Diagnosis is clinical as there are no diagnostic tests

Features

- visual impairment - 'blurred vision' etc

Fundoscopy

- characteristic appearance showing retinal haemorrhages and necrosis
- often called 'pizza' retina

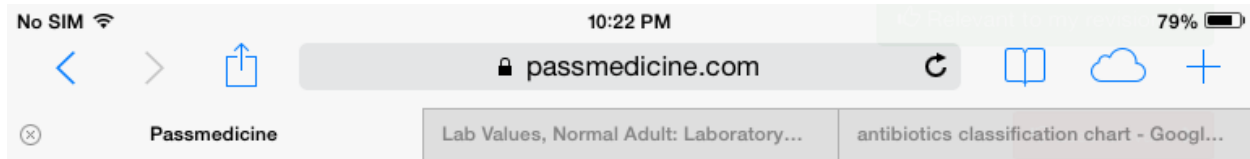


Fundus photograph showing CMV retinitis. Credit: National Eye Institute, National Institutes of Health

Management

- IV ganciclovir
- treatment used to be life-long but new evidence suggests that it may be discontinued once CD4 > 150 after HAART
- alternative: IV foscarnet or cidofovir

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HIV: anti-retrovirals

Highly active anti-retroviral therapy (HAART) involves a combination of at least three drugs, typically two nucleoside reverse transcriptase inhibitors (NRTI) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination both decreases viral replication but also reduces the risk of viral resistance emerging

Following the 2015 BHIVA guidelines it is now recommended that patients start HAART as soon as they have been diagnosed with HIV, rather than waiting until a particular CD4 count, as was previously advocated.

Entry inhibitors (CCR5 receptor antagonists)

- maraviroc, enfuvirtide
- prevent HIV-1 from entering and infecting immune cells by blocking CCR5 cell-surface receptor

Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), abacavir, emtricitabine, didanosine, lamivudine, stavudine, zalcitabine, tenofovir
- general NRTI side-effects: peripheral neuropathy
- zidovudine: anaemia, myopathy, black nails
- didanosine: pancreatitis

Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz
- side-effects: P450 enzyme interaction (nevirapine induces), rashes

Protease inhibitors (PI)

- examples: indinavir, nelfinavir, ritonavir, saquinavir
- side-effects: diabetes, hyperlipidaemia, buffalo hump, central obesity, P450 enzyme inhibition
- indinavir: renal stones, asymptomatic hyperbilirubinaemia
- ritonavir: a potent inhibitor of the P450 system

Integrase inhibitors

- examples: raltegravir, elvitegravir, dolutegravir

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HIV: *Pneumocystis jiroveci* pneumonia

Whilst the organism *Pneumocystis carinii* is now referred to as *Pneumocystis jiroveci*, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use

- *Pneumocystis jiroveci* is an unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in AIDS
- all patients with a CD4 count $< 200/\text{mm}^3$ should receive PCP prophylaxis

Features

- dyspnoea
- dry cough
- fever
- very few chest signs

Pneumothorax is a common complication of PCP.

Extrapulmonary manifestations are rare (1-2% of cases), may cause

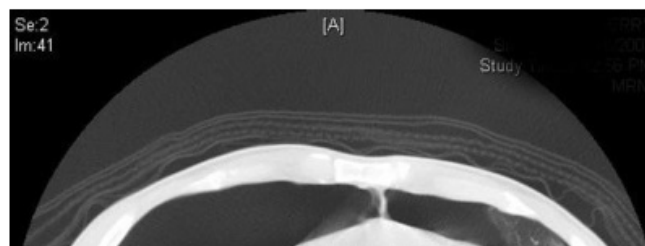
- hepatosplenomegaly
- lymphadenopathy
- choroid lesions

Investigation

- CXR: typically shows bilateral interstitial pulmonary infiltrates but can present with other x-ray findings e.g. lobar consolidation. May be normal
- exercise-induced desaturation
- sputum often fails to show PCP, bronchoalveolar lavage (BAL) often needed to demonstrate PCP (silver stain shows characteristic cysts)

Management

- co-trimoxazole
- IV pentamidine in severe cases
- steroids if hypoxic (if $\text{pO}_2 < 9.3\text{kPa}$ then steroids reduce risk of respiratory failure by 50% and death by a third)





HIV: Kaposi's sarcoma



Kaposi's sarcoma

- caused by HHV-8 (human herpes virus 8)
- presents as purple papules or plaques on the skin or mucosa (e.g. gastrointestinal and respiratory tract)
- skin lesions may later ulcerate
- respiratory involvement may cause massive haemoptysis and pleural effusion
- radiotherapy + resection



Kaposi's sarcoma in a patient with HIV

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DermlS.net

[Picture of Kaposi's sarcoma](#)

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HIV: opportunistic infections and other disorders

The table below shows the infections and other disorders that may be encountered by patients with HIV according to the CD4 count.

CD4 count 200 - 500 cells/mm³

Disorder	Notes
Oral thrush	Secondary to <i>Candida albicans</i>
Shingles	Secondary to herpes zoster
Hairy leukoplakia	Secondary to EBV
Kaposi sarcoma	Secondary to HHV-8

CD4 count 100 - 200 cells/mm³

Disorder	Notes
Cryptosporidiosis	Whilst patients with a CD4 count of 200-500 may develop cryptosporidiosis the disease is usually self-limiting and similar to that in immunocompetent hosts
Cerebral toxoplasmosis	
Progressive multifocal leukoencephalopathy	Secondary to the JC virus
<i>Pneumocystis jirovecii</i> pneumonia	
HIV dementia	

CD4 count 50 - 100 cells/mm³

Disorder	Notes
Aspergillosis	Secondary to <i>Aspergillus fumigatus</i>
Oesophageal candidiasis	Secondary to <i>Candida albicans</i>

CD4 count 50 - 100 cells/mm³

Disorder	Notes
Aspergillosis	Secondary to <i>Aspergillus fumigatus</i>
Oesophageal candidiasis	Secondary to <i>Candida albicans</i>
Cryptococcal meningitis	
Primary CNS lymphoma	Secondary to EBV

CD4 count < 50 cells/mm³

Disorder	Notes
Cytomegalovirus retinitis	Affects around 30-40% of patients with CD4 < 50 cells/mm ³
Mycobacterium avium-intracellulare infection	

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HIV: neurocomplications

Focal neurological lesions

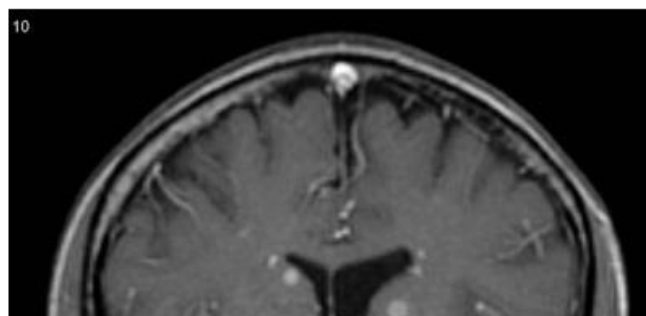
Toxoplasmosis

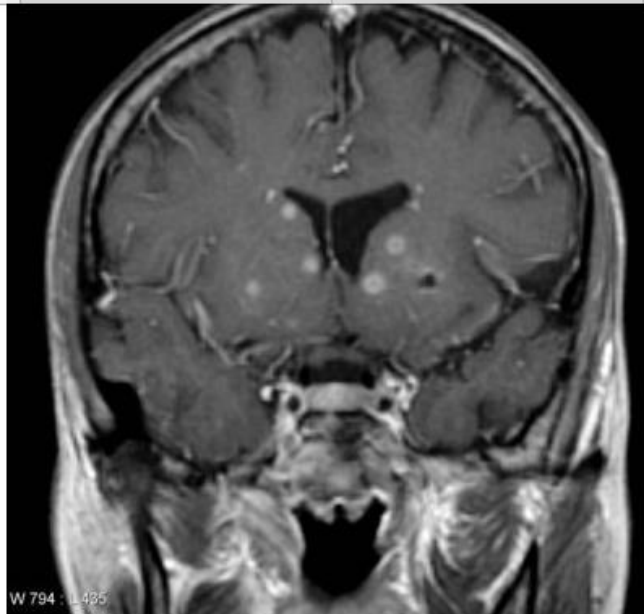
- accounts for around 50% of cerebral lesions in patients with HIV
- constitutional symptoms, headache, confusion, drowsiness
- CT: usually single or multiple ring enhancing lesions, mass effect may be seen
- management: sulfadiazine and pyrimethamine



© Image used on license from Radiopaedia

Cerebral toxoplasmosis: CT scan with contrast showing multiple ring enhancing lesions





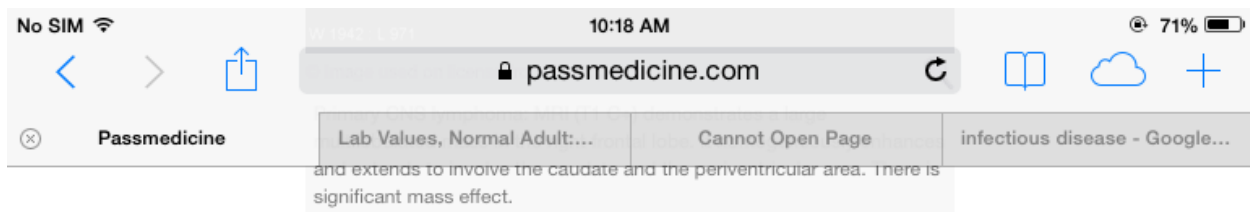
© Image used on license from Radiopaedia

Cerebral toxoplasmosis: MRI (T1 C+) demonstrates multiple small peripherally enhancing nodules located predominantly in the basal ganglia as well as the central portions of the cerebellar hemispheres. Only a small amount of surrounding oedema is present.

Primary CNS lymphoma

- accounts for around 30% of cerebral lesions
- associated with the Epstein-Barr virus
- CT: single or multiple homogenous enhancing lesions
- treatment generally involves steroids (may significantly reduce tumour size), chemotherapy (e.g. methotrexate) + with or without whole brain irradiation. Surgical may be considered for lower grade tumours





Differentiating between toxoplasmosis and lymphoma is a common clinical scenario in HIV patients. It is clearly important given the vastly different treatment strategies. The table below gives some general differences. Please see the Radiopaedia link for more details.

Toxoplasmosis	Lymphoma
Multiple lesions	Single lesion
Ring or nodular enhancement	Solid (homogenous) enhancement
Thallium SPECT negative	Thallium SPECT positive

Tuberculosis

- much less common than toxoplasmosis or primary CNS lymphoma
- CT: single enhancing lesion

Generalised neurological disease

Encephalitis

- may be due to CMV or HIV itself
- HSV encephalitis but is relatively rare in the context of HIV
- CT: oedematous brain

Cryptococcus

- most common fungal infection of CNS
- headache, fever, malaise, nausea/vomiting, seizures, focal neurological deficit
- CSF: high opening pressure, India ink test positive
- CT: meningeal enhancement, cerebral oedema
- meningitis is typical presentation but may occasionally cause a space occupying lesion

Progressive multifocal leukoencephalopathy (PML)

- widespread demyelination
- due to infection of oligodendrocytes by JC virus (a polyoma DNA virus)
- symptoms, subacute onset : behavioural changes, speech, motor, visual impairment
- CT: single or multiple lesions, no mass effect, don't usually enhance. MRI is better - high-signal demyelinating white matter lesions are seen

AIDS dementia complex

- caused by HIV virus itself
- symptoms: behavioural changes, motor impairment
- CT: cortical and subcortical atrophy



Next question >

HIV: diarrhoea

Diarrhoea is common in patients with HIV. This may be due to the effects of the virus itself (HIV enteritis) or opportunistic infections

Possible causes

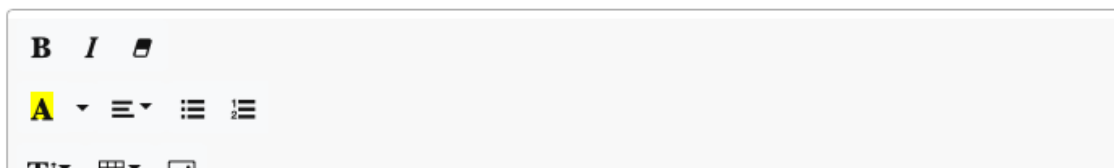
- Cryptosporidium + other protozoa (most common)
- Cytomegalovirus
- *Mycobacterium avium intracellulare*
- Giardia

Cryptosporidium is the most common infective cause of diarrhoea in HIV patients. It is an intracellular protozoa and has an incubation period of 7 days. Presentation is very variable, ranging from mild to severe diarrhoea. A modified Ziehl-Neelsen stain (acid-fast stain) of the stool may reveal the characteristic red cysts of Cryptosporidium. Treatment is difficult, with the mainstay of management being supportive therapy*

Mycobacterium avium intracellulare is an atypical mycobacteria seen with the CD4 count is below 50. Typical features include fever, sweats, abdominal pain and diarrhoea. There may be hepatomegaly and deranged LFTs. Diagnosis is made by blood cultures and bone marrow examination. Management is with rifabutin, ethambutol and clarithromycin

*nitazoxanide is licensed in the US for immunocompetent patients

Next question >



Animal bites

The majority of bites seen in everyday practice involve dogs and cats. These are generally polymicrobial but the most common isolated organism is *Pasteurella multocida*.

Management

- cleanse wound
- current BNF recommendation is co-amoxiclav
- if penicillin-allergic then doxycycline + metronidazole is recommended

Rabies

Rabies is a viral disease that causes an acute encephalitis. The rabies virus is classed as a RNA rhabdovirus (specifically a lyssavirus) and has a bullet-shaped capsid. The vast majority of cases are caused by dog bites but it may also be transmitted by bat, raccoon and skunk bites. Following a bite the virus travels up the nerve axons towards the central nervous system in a retrograde fashion.

Rabies is estimated to still kill around 25,000-50,000 people across the world each year. The vast majority of the disease burden falls on people in poor rural areas of Africa and Asia. Children are particularly at risk.

Features

- prodrome: headache, fever, agitation
- hydrophobia: water-provoking muscle spasms
- hypersalivation
- Negri bodies: cytoplasmic inclusion bodies found in infected neurons

There is now considered to be 'no risk' of developing rabies following an animal bite in the UK and the majority of developed countries. Following an animal bite in at-risk countries:

- the wound should be washed
- if an individual is already immunised then 2 further doses of vaccine should be given
- if not previously immunised then human rabies immunoglobulin (HRIG) should be given along with a full course of vaccination. If possible, the dose should be administered locally around the wound

If untreated the disease is nearly always fatal.

Next question >

Infectious mononucleosis

Infectious mononucleosis (glandular fever) is caused by the Epstein-Barr virus (EBV, also known as human herpesvirus 4, HHV-4) in 90% of cases. Less frequent causes include cytomegalovirus and HHV-6. It is most common in adolescents and young adults.

The classic triad of sore throat, pyrexia and lymphadenopathy is seen in around 98% of patients:

- sore throat
- lymphadenopathy: may be present in the anterior and posterior triangles of the neck, in contrast to tonsillitis which typically only results in the upper anterior cervical chain being enlarged
- pyrexia

Other features include:

- malaise, anorexia, headache
- palatal petechiae
- splenomegaly - occurs in around 50% of patients and may rarely predispose to splenic rupture
- hepatitis, transient rise in ALT
- lymphocytosis: presence of 50% lymphocytes with at least 10% atypical lymphocytes
- haemolytic anaemia secondary to cold agglutins (IgM)
- a maculopapular, pruritic rash develops in around 99% of patients who take ampicillin/amoxicillin whilst they have infectious mononucleosis

Symptoms typically resolve after 2-4 weeks.

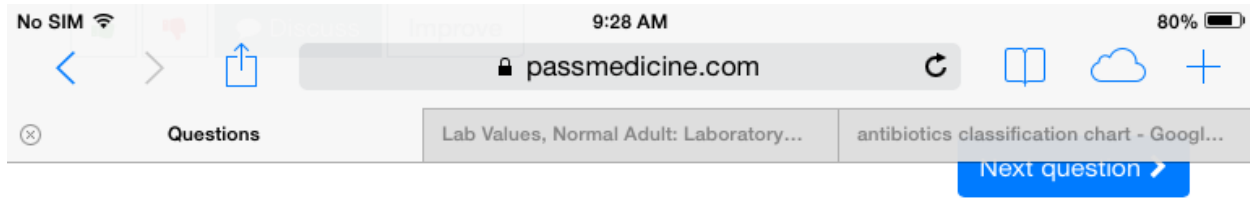
Diagnosis

- heterophil antibody test (Monospot test) - NICE guidelines suggest FBC and Monospot in the 2nd week of the illness to confirm a diagnosis of glandular fever.

Management is supportive and includes:

- rest during the early stages, drink plenty of fluid, avoid alcohol
- simple analgesia for any aches or pains
- consensus guidance in the UK is to avoid playing contact sports for 8 weeks after having glandular fever to reduce the risk of splenic rupture

There is an interesting correlation between EBV and socioeconomic groups. Lower socioeconomic groups have high rates of EBV seropositivity, having frequently acquired EBV in early childhood when the primary infection is often subclinical. However, higher socioeconomic groups show a higher incidence of infectious mononucleosis, as acquiring EBV in adolescence or early adulthood results in symptomatic disease.



H1N1 influenza pandemic

The 2009 H1N1 influenza (swine flu) outbreak was first observed in Mexico in early 2009. In June 2009, the WHO declared the outbreak to be a pandemic.

H1N1

The H1N1 virus is a subtype of the influenza A virus and the most common cause of flu in humans. The 2009 pandemic was caused by a new strain of the H1N1 virus.

The following groups are particularly at risk:

- patients with chronic illnesses and those on immunosuppressants
- pregnant women
- young children under 5 years old

Features

The majority of symptoms are typical of those seen in a flu-like illness:

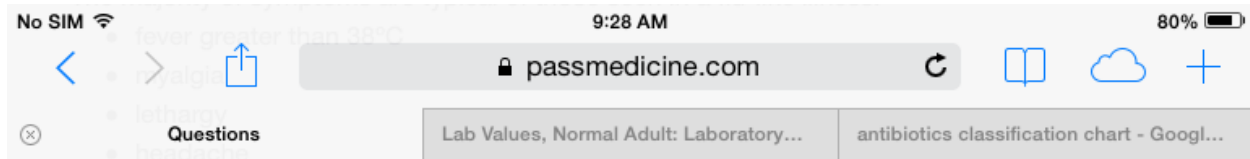
- fever greater than 38°C
- myalgia
- lethargy
- headache
- rhinitis
- sore throat
- cough
- diarrhoea and vomiting

A minority of patients may go on to develop an acute respiratory distress syndrome which may require ventilatory support.

Treatment

There are two main treatments currently available:

Oseltamivir (Tamiflu)



- rhinitis
- sore throat
- cough
- diarrhoea and vomiting

A minority of patients may go on to develop an acute respiratory distress syndrome which may require ventilatory support.

Treatment

There are two main treatments currently available:

Oseltamivir (Tamiflu)

- oral medication
- a neuraminidase inhibitor which prevents new viral particles from being released by infected cells
- common side-effects include nausea, vomiting, diarrhoea and headaches

Zanamivir (Relenza)

- inhaled medication*
- also a neuraminidase inhibitor
- may induce bronchospasm in asthmatics

*intravenous preparations are available for patients who are acutely unwell

Next question >



Dengue fever

Dengue fever is a viral infection which can progress to viral haemorrhagic fever (also yellow fever, Lassa fever, Ebola)

Basics

- transmitted by the *Aedes aegypti* mosquito
- incubation period of 7 days
- a form of disseminated intravascular coagulation (DIC) known as dengue haemorrhagic fever (DHF) may develop. Around 20-30% of these patients go on to develop dengue shock syndrome (DSS)

Features

- causes headache (often retro-orbital)
- fever
- myalgia
- pleuritic pain
- facial flushing (dengue)
- maculopapular rash

Treatment is entirely symptomatic e.g. fluid resuscitation, blood transfusion etc

[Next question >](#)

Chikungunya

Alphavirus disease caused by infected mosquitoes. Areas affected are Africa, Asia and Indian subcontinent but in recent years there has been seen in a few cases in Southern Europe. Tanzania had the first reported case.

Symptoms: Prominent symptoms are severe joint pain and abrupt onset of high fever. Other symptoms include general flu-like illness of muscle ache, headache, and fatigue. The disease shares its symptoms with dengue but tends to have more joint pain which can be debilitating. A rash may develop as with other viral illness and swelling of the joints is not uncommon.

Treatment: Relief of symptoms. No specific treatment.

[Next question >](#)

Yellow fever



Which one

Heart b

Atypica

Hypona

Eryther

Spleno

Eryther

Type of viral haemorrhagic fever (also dengue fever, Lassa fever, Ebola).

Basics

- spread by *Aedes* mosquitos
- incubation period = 2 - 14 days

Features

- may cause mild flu-like illness lasting less than one week
- classic description involves sudden onset of high fever, rigors, nausea & vomiting. Bradycardia may develop. A brief remission is followed by jaundice, haematemesis, oliguria
- if severe jaundice, haematemesis may occur
- Councilman bodies (inclusion bodies) may be seen in the hepatocytes



Zika virus

Zika is a mosquito-borne infection caused by Zika virus, a member of the genus flavivirus and family Flaviviridae. It was first isolated from a monkey in the Zika forest in Uganda in 1947.

Transmission is usually via the bite of an infected Aedes mosquito, although a small number of cases of sexual transmission have been reported. There is increasing evidence of transmission via the placenta from mother to fetus.

The majority of people infected with Zika virus have no symptoms. For those with symptoms, Zika virus tends to cause a mild, short-lived (2 to 7 days) febrile disease. Signs and symptoms suggestive of Zika virus infection may include a combination of the following:

- fever
- rash
- arthralgia/arthritis
- conjunctivitis
- myalgia
- headache
- retro-orbital pain
- pruritus

Serious complications in adults are not common, although the virus has been associated with Guillain-Barre syndrome. Scientific consensus however has linked Zika with microcephaly and other congenital abnormalities, which has led the World Health Organisation (WHO) to declare a Public Health Emergency of International Concern (PHEIC).

Advice for travellers

There is currently no vaccine or drug to prevent Zika infection. Prevention revolves around avoiding mosquito bites (Aedes mosquitoes usually bite during the day) by using mosquito repellent and cover up clothing. Pregnant women are advised to avoid non-essential travel to Zika prevalent areas until after pregnancy.

Next question >

Orf

Orf is generally a condition found in sheep and goats although it can be transmitted to humans. It is caused by the parapox virus.

In animals

- 'scabby' lesions around the mouth and nose

In humans

- generally affects the hands and arms
- initially small, raised, red-blue papules
- later may increase in size to 2-3 cm and become flat-topped and haemorrhagic

Next question >

Parvovirus B19

Parvovirus B19 is a DNA virus which causes a variety of clinical presentations. It was identified in the 1980's as the cause of erythema infectiosum

Erythema infectiosum (also known as fifth disease or 'slapped-cheek syndrome')

The illness may consist of a mild feverish illness which is hardly noticeable. However, in others there is a noticeable rash which appears after a few days. The rose-red rash makes the cheeks appear bright red, hence the name 'slapped cheek syndrome'. The rash may spread to the rest of the body but unlike many other rashes, it only rarely involves the palms and soles.

The child begins to feel better as the rash appears and the rash usually peaks after a week and then fades. The rash is unusual in that for some months afterwards, a warm bath, sunlight, heat or fever will trigger a recurrence of the bright red cheeks and the rash itself. Most children recover and need no specific treatment. In adults, the virus may cause acute arthritis.

Be aware that the virus can affect an unborn baby in the first 20 weeks of pregnancy. If a woman is exposed early in pregnancy (before 20 weeks) she should seek prompt advice from whoever is giving her antenatal care.

It is spread by the respiratory route and a person is infectious 3 to 5 days before the appearance of the rash. Children are no longer infectious once the rash appears and there is no specific treatment.

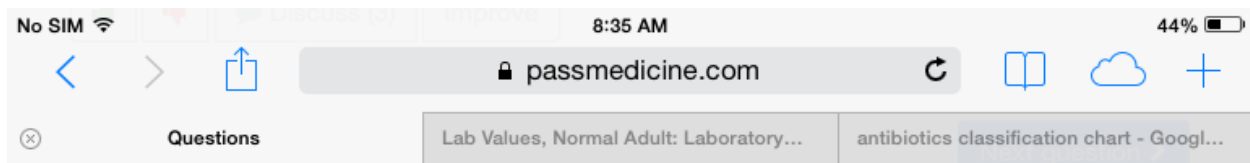
The child need not be excluded from school as they are no longer infectious by the time the rash occurs.

Other presentations

Other presentations include:

- asymptomatic
- pancytopenia in immunosuppressed patients
- aplastic crises e.g. in sickle-cell disease (parvovirus B19 suppresses erythropoiesis for about a week so aplastic anaemia is rare unless there is a chronic haemolytic anaemia)

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Chickenpox exposure in pregnancy

Chickenpox is caused by primary infection with varicella zoster virus. Shingles is reactivation of dormant virus in dorsal root ganglion. In pregnancy there is a risk to both the mother and also the fetus, a syndrome now termed fetal varicella syndrome

Risks to the mother

- 5 times greater risk of pneumonitis

Fetal varicella syndrome (FVS)

- risk of FVS following maternal varicella exposure is around 1% if occurs before 20 weeks gestation
- studies have shown a very small number of cases occurring between 20-28 weeks gestation and none following 28 weeks
- features of FVS include skin scarring, eye defects (microphthalmia), limb hypoplasia, microcephaly and learning disabilities

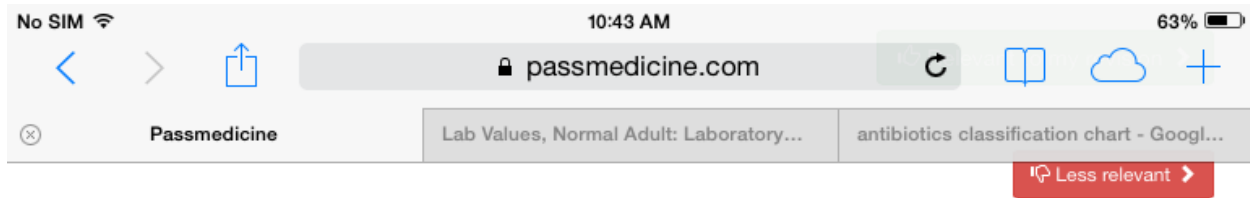
Other risks to the fetus

- shingles in infancy: 1-2% risk if maternal exposure in the second or third trimester
- severe neonatal varicella: if mother develops rash between 5 days before and 2 days after birth there is a risk of neonatal varicella, which may be fatal to the newborn child in around 20% of cases

Management of chickenpox exposure

- if there is any doubt about the mother previously having chickenpox maternal blood should be urgently checked for varicella antibodies
- if the pregnant woman is not immune to varicella she should be given varicella zoster immunoglobulin (VZIG) as soon as possible. RCOG and Greenbook guidelines suggest VZIG is effective up to 10 days post exposure
- consensus guidelines suggest oral aciclovir should be given if pregnant women with chickenpox present within 24 hours of onset of the rash

Next question >



Rubella and pregnancy

Rubella, also known as German measles, is a viral infection caused by the togavirus. Following the introduction of the MMR vaccine it is now rare. If contracted during pregnancy there is a risk of congenital rubella syndrome. Remember that the incubation period is 14-21 days and individuals are infectious from 7 days before symptoms appear to 4 days after the onset of the rash.

Risk

- in first 8-10 weeks risk of damage to fetus is as high as 90%
- damage is rare after 16 weeks

Features of congenital rubella syndrome

- sensorineural deafness
- congenital cataracts
- congenital heart disease (e.g. patent ductus arteriosus)
- growth retardation
- hepatosplenomegaly
- purpuric skin lesions
- 'salt and pepper' chorioretinitis
- microphthalmia
- cerebral palsy

Diagnosis

- suspected cases should be discussed immediately with the local Health Protection Unit (HPU) as type/timing of investigations may vary
- IgM antibodies are raised in women recently exposed to the virus
- it should be noted that it is very difficult to distinguish rubella from parvovirus B19 clinically. It is therefore important to also check parvovirus B19 serology as there is a 30% risk of transplacental infection, with a 5-10% risk of fetal loss

Management

- women normally have their immunity checked before becoming pregnant
- rubella immunity is routinely checked at the booking visit. If the no immunity is demonstrated pregnant women need to keep away from people who might have rubella
- non-immune mothers should be offered the MMR vaccination in the post-natal period



Antifungal agents

Drug	Mechanism of action	Adverse effects	Notes
Azoles	Inhibits 14 α -demethylase which produces ergosterol	P450 inhibition Liver toxicity	
Amphotericin B	Binds with ergosterol forming a transmembrane channel that leads to monovalent ion (K ⁺ , Na ⁺ , H ⁺ and Cl ⁻) leakage	Nephrotoxicity, flu-like symptoms, hypokalaemia, hypomagnasaemia	Used for systemic fungal infections
Terbinafine	Inhibits squalene epoxidase		Commonly used in oral form to treat fungal nail infections
Griseofulvin	Interacts with microtubules to disrupt mitotic spindle	Induces P450 system, teratogenic	
Flucytosine	Converted by cytosine deaminase to 5-fluorouracil, which inhibits thymidylate synthase and disrupts fungal protein synthesis	Vomiting	
Caspofungin	Inhibits synthesis of beta-glucan, a major fungal cell wall component	Flushing	
Nystatin	Binds with ergosterol forming a transmembrane channel that leads to monovalent ion (K ⁺ , Na ⁺ , H ⁺ and Cl ⁻) leakage		As very toxic can only be used topically (e.g. for oral thrush)

Aspergilloma

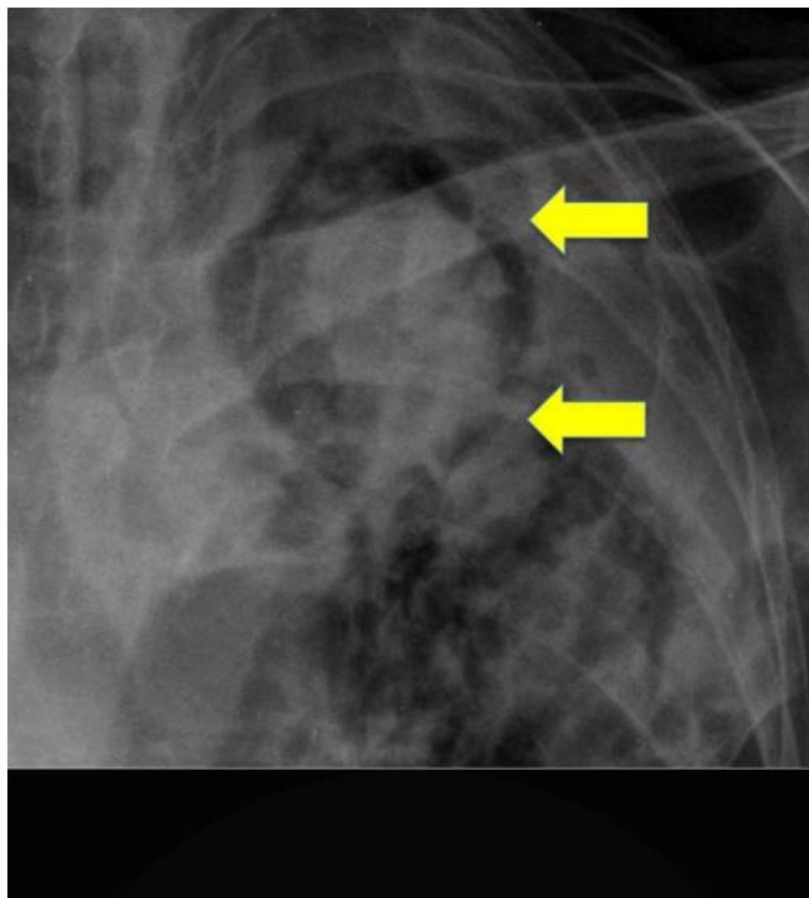
An aspergilloma is a mycetoma (mass-like fungus ball) which often colonises an existing lung cavity (e.g. secondary to tuberculosis, lung cancer or cystic fibrosis)

Usually asymptomatic but features may include

- cough
- haemoptysis (may be severe)

Investigations

- chest x-ray containing a rounded opacity
- high titres *Aspergillus* precipitins



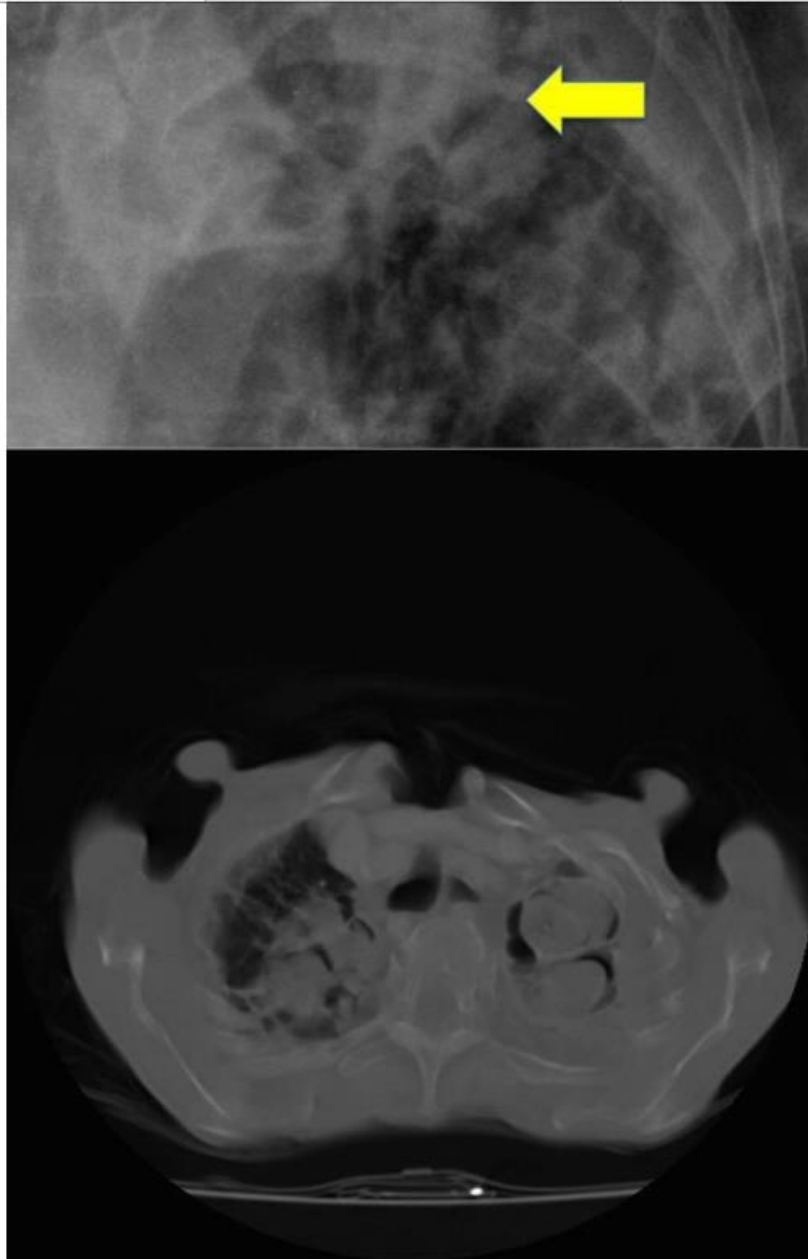


Image used on license from Radiopaedia

Aspergilloma in a patient with cavities secondary to previous tuberculosis infection. The close-up CXR and CT scan from the same patient demonstrate a rounded soft tissue attenuating masses located in a surrounding cavity.

Next question >

Amoebiasis

Amoebiasis is caused by *Entamoeba histolytica* (an amoeboid protozoan) and spread by the faecal-oral route. It is estimated that 10% of the world's population is chronically infected. Infection can be asymptomatic, cause mild diarrhoea or severe amoebic dysentery. Amoebiasis also causes liver and colonic abscesses

Amoebic dysentery

- profuse, bloody diarrhoea
- stool microscopy may show trophozoites
- treatment is with metronidazole

Amoebic liver abscess

- usually a single mass in the right lobe (may be multiple)
- features: fever, RUQ pain
- serology is positive in > 90%

Next question >

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Trypanosomiasis

Question

Two main form of this protozoal disease are recognised - African trypanosomiasis (sleeping sickness) and American trypanosomiasis (Chagas' disease)

Granuloma

Primary

Secondary

Tertiary

Congenital

Two forms of **African trypanosomiasis**, or **sleeping sickness**, are seen - *Trypanosoma gambiense* in West Africa and *Trypanosoma rhodesiense* in East Africa. Both types are spread by the tsetse fly. *Trypanosoma rhodesiense* tends to follow a more acute course. Clinical features include:

- Trypanosoma chancre - painless subcutaneous nodule at site of infection
- intermittent fever
- enlargement of posterior cervical lymph nodes
- later: central nervous system involvement e.g. somnolence, headaches, mood changes, meningoencephalitis

Management

- early disease: IV pentamidine or suramin
- later disease or central nervous system involvement: IV melarsoprol

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American trypanosomiasis, or **Chagas' disease**, is caused by the protozoan *Trypanosoma cruzi*. The vast majority of patients (95%) are asymptomatic in the acute phase although a chagoma (an erythematous nodule at site of infection) and periorbital oedema are sometimes seen. Chronic Chagas' disease mainly affects the heart and gastrointestinal tract

- myocarditis may lead to dilated cardiomyopathy (with apical atrophy) and arrhythmias
- gastrointestinal features includes megaesophagus and megacolon causing dysphagia and constipation

Dilated

Management

- treatment is most effective in the acute phase using azole or nitroderivatives such as benznidazole or nifurtimox
- chronic disease management involves treating the complications e.g., heart failure

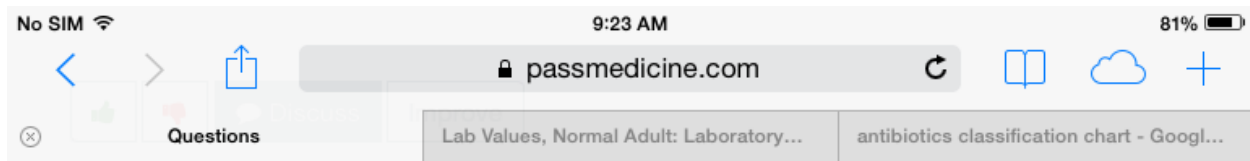
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Toxoplasmosis

Toxoplasma gondii is a protozoa which infects the body via the GI tract, lung or broken skin. It's oocysts release trophozoites which migrate widely around the body including to the eye, brain and muscle. The usual animal reservoir is the cat, although other animals such as rats carry the disease.

Most infections are asymptomatic. Symptomatic patients usually have a self-limiting infection, often having clinical features resembling infectious mononucleosis (fever, malaise, lymphadenopathy). Other less common manifestations include meningoencephalitis and myocarditis.

Investigation

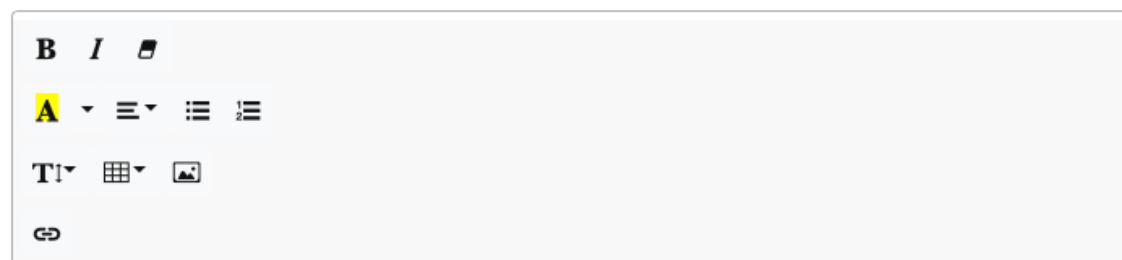
- antibody test
- Sabin-Feldman dye test

Treatment is usually reserved for those with severe infections or patients who are immunosuppressed

- pyrimethamine plus sulphadiazine for at least 6 weeks

Congenital toxoplasmosis is due to transplacental spread from the mother. It causes a variety of effects to the unborn child including microcephaly, hydrocephalus, cerebral calcification and choroidoretinitis.

Next question >



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Questions Lab Values, Normal Adult: Laboratory... antibiotics classification chart - Googl...

Discuss Improve

Next question >

Leishmaniasis

Leishmaniasis is caused by the intracellular protozoa *Leishmania*, usually being spread by sand flies. Cutaneous, mucocutaneous leishmaniasis and visceral forms are seen

Cutaneous leishmaniasis

- caused by *Leishmania tropica* or *Leishmania mexicana*
- crusted lesion at site of bite
- may be underlying ulcer

Mucocutaneous leishmaniasis

- caused by *Leishmania braziliensis*
- skin lesions may spread to involve mucosae of nose, pharynx etc

Visceral leishmaniasis (kala-azar)

- mostly caused by *Leishmania donovani*
- occurs in the Mediterranean, Asia, South America, Africa
- fever, sweats, rigors
- massive splenomegaly. hepatomegaly
- poor appetite*, weight loss
- grey skin - 'kala-azar' means black sickness
- pancytopenia secondary to hypersplenism

*occasionally patients may report increased appetite with paradoxical weight loss

Next question >

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Questions Lab Values, Normal Adult: Laboratory... antibiotics classification chart - Googl...

Discuss Improve

Next question >

Nematodes

Ancylostoma braziliense

- most common cause of cutaneous larva migrans
- common in Central and Southern America

Strongyloides stercoralis

- acquired percutaneously (e.g. walking barefoot)
- causes pruritus and larva currens - this has a similar appearance to cutaneous larva migrans but moves through the skin at a far greater rate
- abdo pain, diarrhoea, pneumonitis
- may cause Gram negative septicaemia due carrying of bacteria into bloodstream
- eosinophilia sometimes seen
- management: thiabendazole, albendazole. Ivermectin also used, particularly in chronic infections

Toxocara canis

- commonly acquired by ingesting eggs from soil contaminated by dog faeces
- commonest cause of visceral larva migrans
- other features: eye granulomas, liver/lung involvement

Next question >

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Next question >

Tape worms

Tape worms are made up of repeated segments called proglottids. These are often present in faeces and are useful diagnostically

Cysticercosis

- caused by *Taenia solium* (from pork) and *Taenia saginata* (from beef)
- management: niclosamide

Hydatid disease

- caused by the dog tapeworm *Echinococcus granulosus*
- life-cycle involves dogs ingesting hydatid cysts from sheep liver
- often seen in farmers
- may cause liver cysts
- management: albendazole

Next question >

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Question 18

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Urinary

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Schistosomiasis

Schistosomiasis, or bilharzia, is a parasitic flatworm infection. The following types of schistosomiasis are recognised:

- Schistosoma mansoni and Schistosoma intercalatum: intestinal schistosomiasis
- Schistosoma haematobium: urinary schistosomiasis

Schistosoma haematobium

This typically presents as a 'swimmer's itch' in patients who have recently returned from Africa. Schistosoma haematobium is a risk factor for squamous cell bladder cancer

Features

- frequency
- haematuria
- bladder calcification

Management

- single oral dose of praziquantel

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Royal College of Physicians

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[2011 Schistosomiasis review](#)



Strongyloides stercoralis

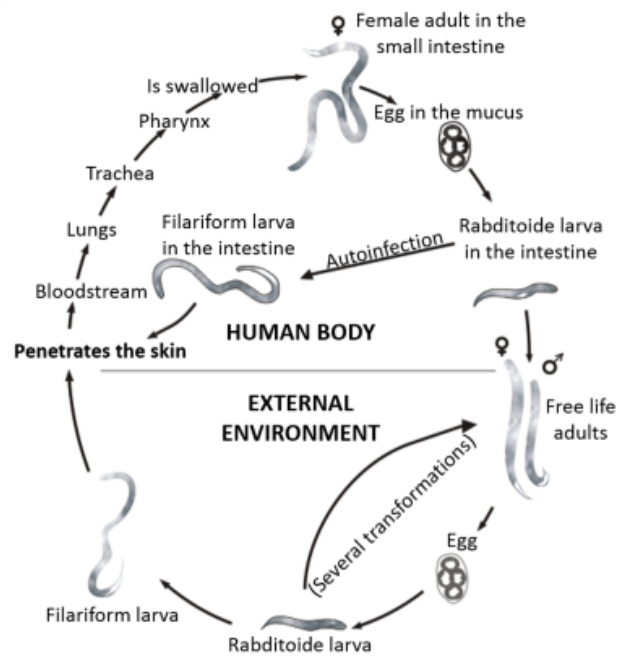
Strongyloides stercoralis is a human parasitic nematode worm. The larvae are present in soil and gain access to the body by penetrating the skin. Infection with *Strongyloides stercoralis* causes strongyloidiasis.

Features

- diarrhoea
- abdominal pain/bloating
- papulovesicular lesions where the skin has been penetrated by infective larvae e.g. soles of feet and buttocks
- larva currens: pruritic, linear, urticarial rash
- if the larvae migrate to the lungs a pneumonitis similar to Loeffler's syndrome may be triggered

Treatment

- ivermectin and albendazole are used



Strongyloides stercoralis Life Cycle, Nematode (Hookworm)

Image sourced from Wikipedia

Diagram showing the lifecycle of *Strongyloides stercoralis*

End session

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Oral or

A 40-year-old

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Next question >

Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer.

Features

- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

Management

- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment and recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

Next question >

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Bacterial vaginosis

Bacterial vaginosis (BV) describes an overgrowth of predominately anaerobic organisms such as *Gardnerella vaginalis*. This leads to a consequent fall in lactic acid producing aerobic lactobacilli resulting in a raised vaginal pH.

Whilst BV is not a sexually transmitted infection it is seen almost exclusively in sexually active women.

Features

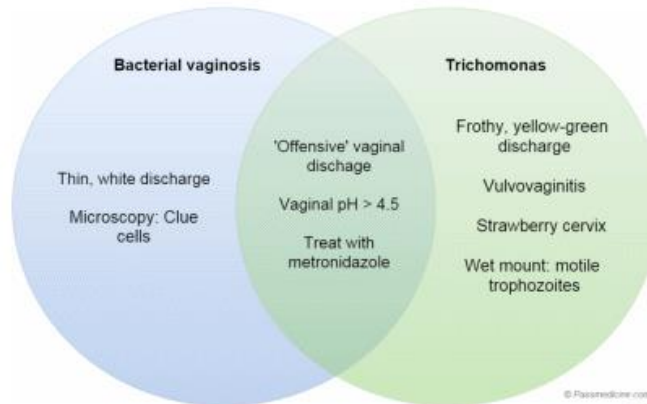
- vaginal discharge: 'fishy', offensive
- asymptomatic in 50%

Amsel's criteria for diagnosis of BV - 3 of the following 4 points should be present

- thin, white homogenous discharge
- clue cells on microscopy: stippled vaginal epithelial cells
- vaginal pH > 4.5
- positive whiff test (addition of potassium hydroxide results in fishy odour)

Management

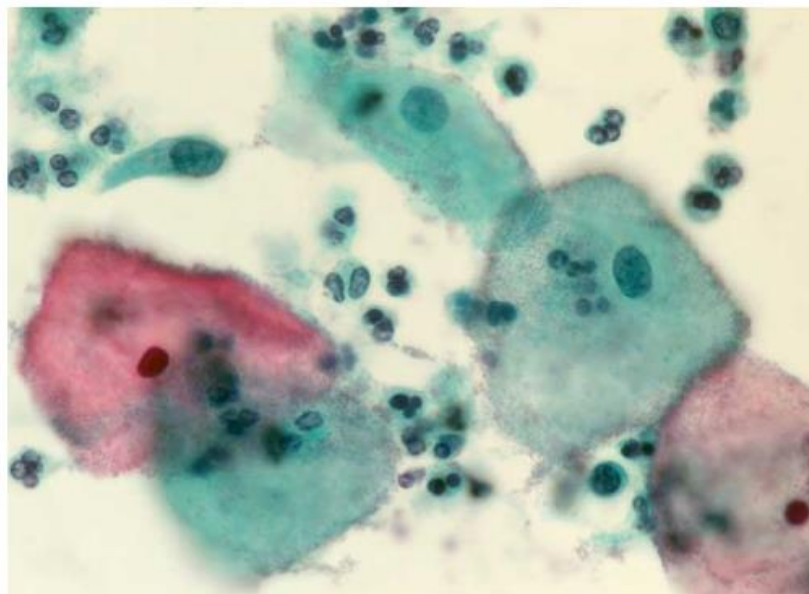
- oral metronidazole for 5-7 days
 - 70-80% initial cure rate
 - relapse rate > 50% within 3 months
 - the BNF suggests topical metronidazole or topical clindamycin as alternatives
- 



Comparison of bacterial vaginosis and *Trichomonas vaginalis*

Bacterial vaginosis in pregnancy

- results in an increased risk of preterm labour, low birth weight and chorioamnionitis, late miscarriage
- it was previously taught that oral metronidazole should be avoided in the first trimester and topical clindamycin used instead. Recent guidelines however recommend that oral metronidazole is used throughout pregnancy. The BNF still advises against the use of high dose metronidazole regimes



© Image used on license from PathoPic

Clue cells - epithelial cells develop a stippled appearance due to being covered with bacteria

Trichomonas vaginalis

Trichomonas vaginalis is a highly motile, flagellated protozoan parasite. Trichomoniasis is a sexually transmitted infection (STI).

Features

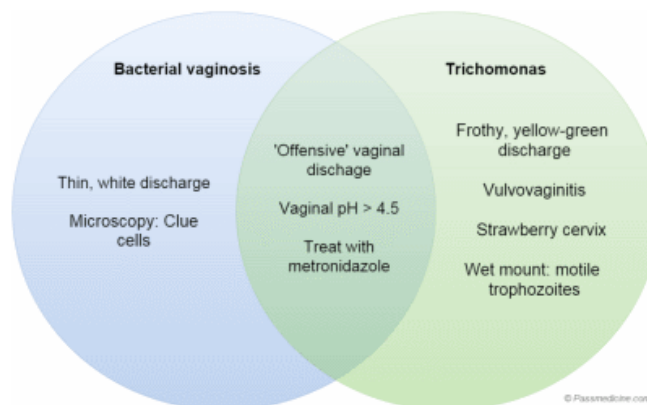
- vaginal discharge: offensive, yellow/green, frothy
- vulvovaginitis
- strawberry cervix
- pH > 4.5
- in men is usually asymptomatic but may cause urethritis

Investigation

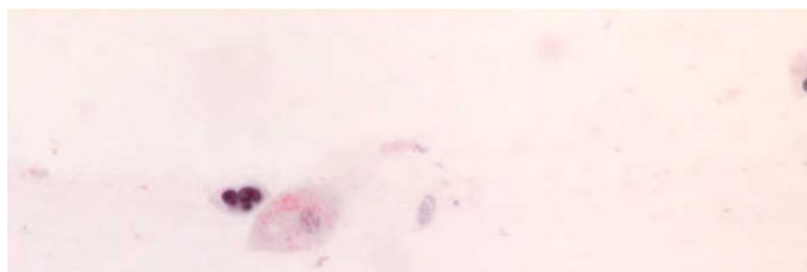
- microscopy of a wet mount shows motile trophozoites

Management

- oral metronidazole for 5-7 days, although the BNF also supports the use of a one-off dose of 2g metronidazole



Comparison of bacterial vaginosis and *Trichomonas vaginalis*



Gonorrhoea

Gonorrhoea is caused by the Gram negative diplococcus *Neisseria gonorrhoeae*. Acute infection can occur on any mucous membrane surface, typically genitourinary but also rectum and pharynx. The incubation period of gonorrhoea is 2-5 days

Features

- males: urethral discharge, dysuria
- females: cervicitis e.g. leading to vaginal discharge
- rectal and pharyngeal infection is usually asymptomatic

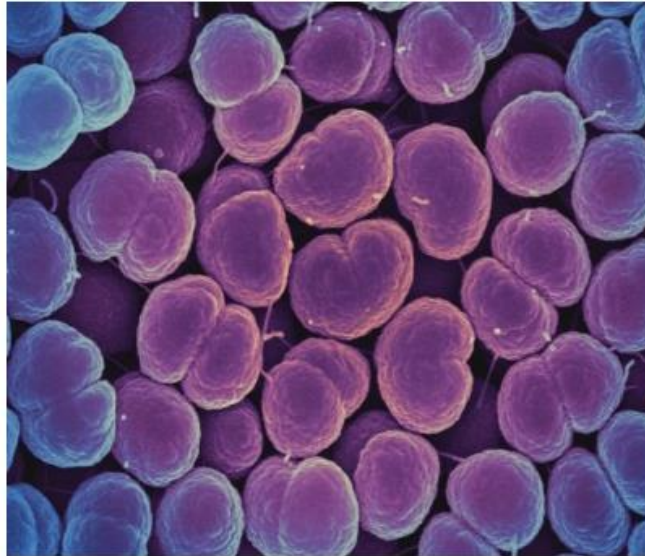
Microbiology

- immunisation is not possible and reinfection is common due to antigen variation of type IV pili (proteins which adhere to surfaces) and Opa proteins (surface proteins which bind to receptors on immune cells)

Local complications that may develop include urethral strictures, epididymitis and salpingitis (hence may lead to infertility). Disseminated infection may occur - see below

Management

- ciprofloxacin used to be the treatment of choice. However, there is increased resistance to ciprofloxacin and therefore cephalosporins are now used
- the 2011 British Society for Sexual Health and HIV (BASHH) guidelines recommend ceftriaxone 500 mg intramuscularly as a single dose with azithromycin 1 g oral as a single dose. The azithromycin is thought to act synergistically with ceftriaxone and is also useful for eradicating any co-existent Chlamydia infections. This combination can be used in pregnant women as well
- if ceftriaxone is refused or contraindicated other options include cefixime 400mg PO (single dose)



Colorized scanning electron micrograph of *Neisseria gonorrhoeae*. Credit: NIAID

Disseminated gonococcal infection (DGI) and gonococcal arthritis may also occur, with gonococcal infection being the most common cause of septic arthritis in young adults. The pathophysiology of DGI is not fully understood but is thought to be due to haematogenous spread from mucosal infection (e.g. Asymptomatic genital infection). Initially there may be a classic triad of symptoms: tenosynovitis, migratory polyarthritits and dermatitis. Later complications include septic arthritis, endocarditis and perihepatitis (Fitz-Hugh-Curtis syndrome)

Key features of disseminated gonococcal infection

- tenosynovitis
- migratory polyarthritits
- dermatitis (lesions can be maculopapular or vesicular)

Next question >

Non-gonococcal urethritis



Question

Hepatitis

May cause

Requires

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Causes

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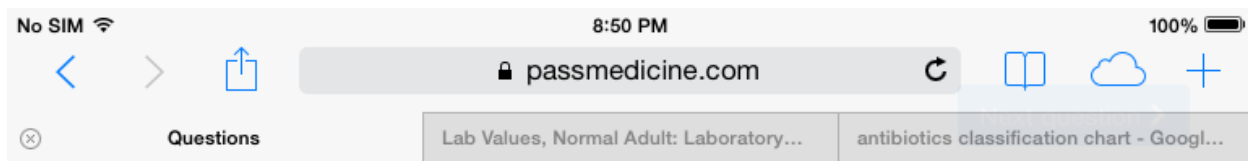
Non-gonococcal urethritis (NGU, sometimes referred to as non-specific urethritis) is a term used to describe the presence of urethritis when a gonococcal bacteria are not identifiable or the initial swab. A typical case would be a male who presented to a GUM clinic with a purulent urethral discharge and dysuria. A swab would be taken in clinic, microscopy performed which showed neutrophils but no Gram negative diplococci (i.e. no evidence of gonorrhoea). Clearly this patient requires immediate treatment prior to waiting for the Chlamydia test to come back and hence an initial diagnosis of NGU is made.

Causative organisms include:

- *Chlamydia trachomatis* - most common cause
- *Mycoplasma genitalium* - thought to cause more symptoms than *Chlamydia*

Management

- contact tracing
- the BNF and British Association for Sexual Health and HIV (BASHH) both recommend either oral azithromycin or doxycycline



Chlamydia

Chlamydia is the most prevalent sexually transmitted infection in the UK and is caused by *Chlamydia trachomatis*, an obligate intracellular pathogen. Approximately 1 in 10 young women in the UK have *Chlamydia*. The incubation period is around 7-21 days, although it should be remembered a large percentage of cases are asymptomatic

Features

- asymptomatic in around 70% of women and 50% of men
- women: cervicitis (discharge, bleeding), dysuria
- men: urethral discharge, dysuria

Potential complications

- epididymitis
- pelvic inflammatory disease
- endometritis
- increased incidence of ectopic pregnancies
- infertility
- reactive arthritis
- perihepatitis (Fitz-Hugh-Curtis syndrome)

Investigation

- traditional cell culture is no longer widely used
- nuclear acid amplification tests (NAATs) are now rapidly emerging as the investigation of choice
- urine (first void urine sample), vulvovaginal swab or cervical swab may be tested using the NAAT technique

Screening

- in England the National *Chlamydia* Screening Programme is open to all men and women aged 15-24 years
- the 2009 SIGN guidelines support this approach, suggesting screening all sexually active patients aged 15-24 years
- relies heavily on opportunistic testing

No SIM 8:52 PM 100%

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Questions Lab Values, Normal Adult: Laboratory... antibiotics classification chart - Googl...

Pap smear demonstrating infected endocervical cells. Red inclusion bodies are typical

Management

- doxycycline (7 day course) or azithromycin (single dose). The 2009 SIGN guidelines suggest azithromycin should be used first-line due to potentially poor compliance with a 7 day course of doxycycline
- if pregnant then azithromycin, erythromycin or amoxicillin may be used. The SIGN guidelines suggest azithromycin 1g stat is the drug of choice 'following discussion of the balance of benefits and risks with the patient'
- patients diagnosed with *Chlamydia* should be offered a choice of provider for initial partner notification - either trained practice nurses with support from GUM, or referral to GUM
- for men with urethral symptoms: all contacts since, and in the four weeks prior to, the onset

of symptoms

- for women and asymptomatic men all partners from the last six months or the most recent sexual partner should be contacted
- contacts of confirmed *Chlamydia* cases should be offered treatment prior to the results of their investigations being known (treat then test)

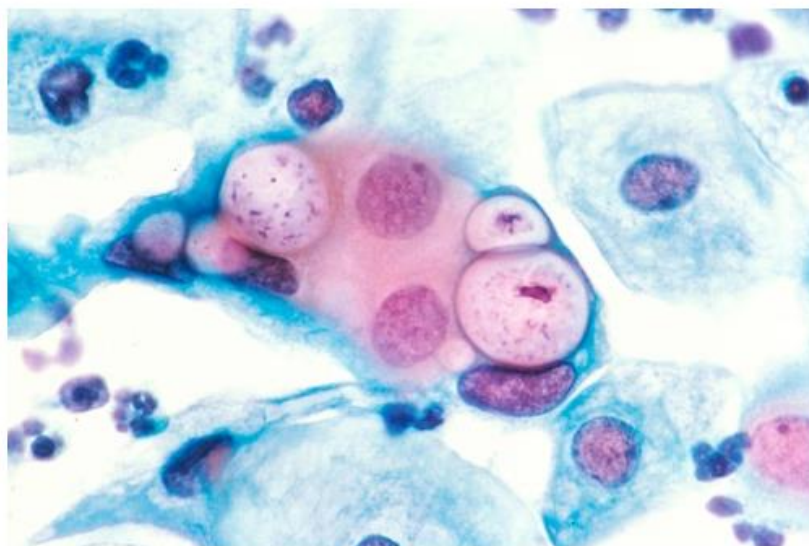


Image sourced from Wikipedia© Image used on license from PathoPic

Another Pap smear demonstrating infected endocervical cells. Stained with H&E

Next question >

Urinary tract infection in adults: management

Lower urinary tract infections

Non-pregnant women

- local antibiotic guidelines should be followed if available
- 2012 SIGN guidelines recommend trimethoprim or nitrofurantoin for 3 days

Pregnant women with symptomatic bacteriuria should be treated with an antibiotic for 7 days. A urine culture should be sent. For asymptomatic pregnant women:

- a urine culture should be performed routinely at the first antenatal visit
- if positive, a second urine culture should be sent to confirm the presence of bacteriuria
- SIGN recommend to treat asymptomatic bacteriuria detected during pregnancy with an antibiotic
- a 7 day course of antibiotics should be given
- a further urine culture should be sent following completion of treatment as a test of cure

Acute pyelonephritis

For patients with sign of acute pyelonephritis hospital admission should be considered

- local antibiotic guidelines should be followed if available
- the BNF currently recommends a broad-spectrum cephalosporin or a quinolone (for non-pregnant women) for 10-14 days

Next question >

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Post-exposure prophylaxis

Hepatitis A

- Human Normal Immunoglobulin (HNIG) or hepatitis A vaccine may be used depending on the clinical situation

Hepatitis B

- HBsAg positive source: if the person exposed is a known responder to HBV vaccine then a booster dose should be given. If they are in the process of being vaccinated or are a non-responder they need to have hepatitis B immune globulin (HBIG) and the vaccine
- unknown source: for known responders the green book advises considering a booster dose of HBV vaccine. For known non-responders HBIG + vaccine should be given whilst those in the process of being vaccinated should have an accelerated course of HBV vaccine

Hepatitis C

- monthly PCR - if seroconversion then interferon +/- ribavirin

HIV

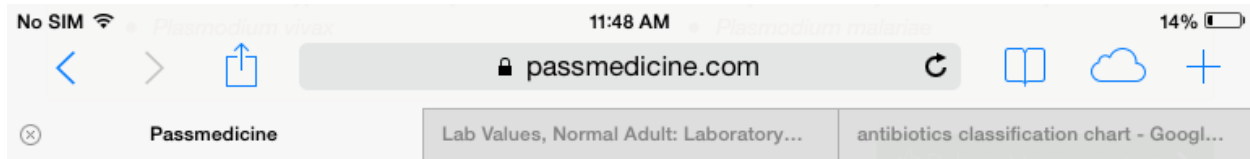
- a combination of oral antiretrovirals (e.g. Tenofovir, emtricitabine, lopinavir and ritonavir) as soon as possible (i.e. Within 1-2 hours, but may be started up to 72 hours following exposure) for 4 weeks
- serological testing at 12 weeks following completion of post-exposure prophylaxis
- reduces risk of transmission by 80%

Varicella zoster

- VZIG for IgG negative pregnant women/immunosuppressed

Estimates of transmission risk for single needlestick injury

Hepatitis B	20-30%
Hepatitis C	0.5-2%
HIV	0.3%



Less relevant >

Malaria: non-falciparum

The most common cause of non-falciparum malaria is *Plasmodium vivax*, with *Plasmodium ovale* and *Plasmodium malariae* accounting for the other cases. *Plasmodium vivax* is often found in Central America and the Indian Subcontinent whilst *Plasmodium ovale* typically comes from Africa

Features

- general features of malaria: fever, headache, splenomegaly
- *Plasmodium vivax/ovale*: cyclical fever every 48 hours. *Plasmodium malariae*: cyclical fever every 72 hours
- *Plasmodium malariae*: is associated with nephrotic syndrome

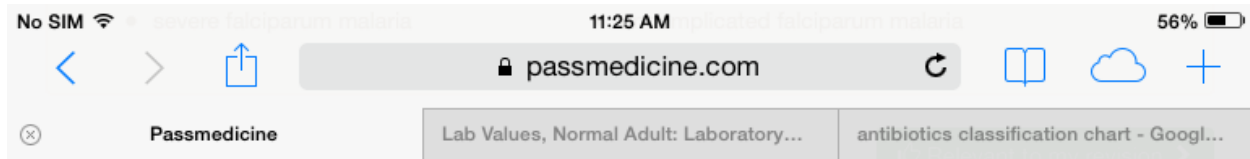
Ovale and vivax malaria have a hypnozoite stage and may therefore relapse following treatment.

Treatment

- in areas which are known to be chloroquine-sensitive then WHO recommend either an artemisinin-based combination therapy (ACT) or chloroquine
- in areas which are known to be chloroquine-resistant an ACT should be used
- ACTs should be avoided in pregnant women
- patients with ovale or vivax malaria should be given primaquine following acute treatment with chloroquine to destroy liver hypnozoites and prevent relapse

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Malaria: Falciparum

Feature of severe malaria

- schizonts on a blood film
- parasitaemia > 2%
- hypoglycaemia
- acidosis
- temperature > 39 °C
- severe anaemia
- complications as below

Complications

- cerebral malaria: seizures, coma
- acute renal failure: blackwater fever, secondary to intravascular haemolysis, mechanism unknown
- acute respiratory distress syndrome (ARDS)
- hypoglycaemia
- disseminated intravascular coagulation (DIC)

Uncomplicated falciparum malaria

- strains resistant to chloroquine are prevalent in certain areas of Asia and Africa
- the 2010 WHO guidelines recommend artemisinin-based combination therapies (ACTs) as first-line therapy
- examples include artemether plus lumefantrine, artesunate plus amodiaquine, artesunate plus mefloquine, artesunate plus sulfadoxine-pyrimethamine, dihydroartemisinin plus piperaquine

Severe falciparum malaria

- a parasite counts of more than 2% will usually need parenteral treatment irrespective of clinical state
- intravenous artesunate is now recommended by WHO in preference to intravenous quinine
- if parasite count > 10% then exchange transfusion should be considered
- shock may indicate coexistent bacterial septicaemia - malaria rarely causes haemodynamic collapse

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Malaria: prophylaxis

There are around 1,500-2,000 cases each year of malaria in patients returning from endemic countries. The majority of these cases (around 75%) are caused by the potentially fatal *Plasmodium falciparum* protozoa. The majority of patients who develop malaria did not take prophylaxis. It should also be remembered that UK citizens who originate from malaria endemic areas quickly lose their innate immunity.

Up-to-date charts with recommended regimes for malarial zones should be consulted prior to prescribing

Drug	Side-effects + notes	Time to begin before travel	Time to end after travel
Atovaquone + proguanil (Malarone)	GI upset	1 - 2 days	7 days
Chloroquine	Headache Contraindicated in epilepsy Taken weekly	1 week	4 weeks
Doxycycline	Photosensitivity Oesophagitis	1 - 2 days	4 weeks
Mefloquine (Lariam)	Dizziness Neuropsychiatric disturbance Contraindicated in epilepsy Taken weekly	2 - 3 weeks	4 weeks
Proguanil (Paludrine)		1 week	4 weeks
Proguanil + chloroquine	See above	1 week	4 weeks

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Questions	Lab Values, Normal Adult: Laboratory...	antibiotics classification chart - Googl...	
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Proguanil + chloroquine	See above	1 week	4 weeks

Pregnant women should be advised to avoid travelling to regions where malaria is endemic. Diagnosis can also be difficult as parasites may not be detectable in the blood film due to placental sequestration. However, if travel cannot be avoided:

- chloroquine can be taken
- proguanil: folate supplementation (5mg od) should be given
- Malarone (atovaquone + proguanil): the BNF advises to avoid these drugs unless essential. If taken then folate supplementation should be given
- mefloquine: caution advised
- doxycycline is contraindicated

It is again advisable to avoid travel to malaria endemic regions with children if avoidable. However, if travel is essential then children should take malarial prophylaxis as they are more at risk of serious complications.

- diethyltoluamide (DEET) 20-50% has been shown to repel up to 100% of mosquitoes if used correctly. It can be used in children over 2 months of age*
- doxycycline is only licensed in the UK for children over the age of 12 years

*A BMJ review (BMJ 2015; 350:h99) suggest DEET could also be used in breastfeeding women and pregnant women in their 2nd or 3rd trimester

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Incubation periods

Questions may either ask directly about incubation periods or they may be used to provide a clue in a differential diagnosis

Less than 1 week

- meningococcus
- diphtheria
- influenza
- scarlet fever

1 - 2 weeks

- malaria
- dengue fever
- typhoid
- measles

2 - 3 weeks

- mumps
- rubella
- chickenpox

Longer than 3 weeks

- infectious mononucleosis
- cytomegalovirus
- viral hepatitis
- HIV

Next question >

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Splenectomy

Following a splenectomy patients are particularly at risk from pneumococcus, Haemophilus, meningococcus and Capnocytophaga canimorsus* infections

Vaccination

- if elective, should be done 2 weeks prior to operation
- Hib, meningitis A & C
- annual influenza vaccination
- pneumococcal vaccine every 5 years

Antibiotic prophylaxis

- penicillin V: unfortunately clear guidelines do not exist of how long antibiotic prophylaxis should be continued. It is generally accepted though that penicillin should be continued for at least 2 years and at least until the patient is 16 years of age, although the majority of patients are usually put on antibiotic prophylaxis for life

Surgical aspects

Indications

- Trauma: 1/4 are iatrogenic
- Spontaneous rupture: EBV
- Hypersplenism: hereditary spherocytosis or elliptocytosis etc
- Malignancy: lymphoma or leukaemia
- Splenic cysts, hydatid cysts, splenic abscesses

Splenectomy following trauma

- GA
- Long midline incision
- If time permits insert a self retaining retractor (e.g. Balfour/ omnitract)
- Large amount of free blood is usually present. Pack all 4 quadrants of the abdomen. Allow the anaesthetist to 'catch up'
- Remove the packs and assess the viability of the spleen. Hilar injuries and extensive parenchymal lacerations will usually require splenectomy.
- Divide the short aastric vessels and liaate them.

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- Divide the short gastric vessels and ligate them.
- Clamp the splenic artery and vein. Two clamps on the patient side are better and allow for double ligation and serve as a safety net if your assistant does not release the clamp smoothly.
- Be careful not to damage the tail of the pancreas, if you do then this will need to be formally removed and the pancreatic duct closed.
- Wash out the abdomen and place a tube drain to the splenic bed.
- Some surgeons implant a portion of spleen into the omentum, whether you decide to do this is a matter of personal choice.
- Postoperatively the patient will require prophylactic penicillin V and pneumococcal vaccine.

Elective splenectomy

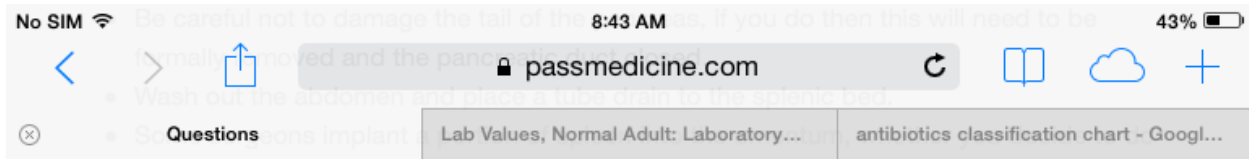
- Elective splenectomy is a very different operation from that performed in the emergency setting. The spleen is often large (sometimes massive)
- Most cases can be performed laparoscopically. The spleen will often be macerated inside a specimen bag to facilitate extraction.

Complications

- Haemorrhage (may be early and either from short gastrics or splenic hilar vessels)
- Pancreatic fistula (from iatrogenic damage to pancreatic tail)
- Thrombocytosis: prophylactic aspirin
- Encapsulated bacteria infection e.g. *Strep. pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis*

Post-splenectomy changes

- Platelets will rise first (therefore in ITP should be given after splenic artery clamped)
- Blood film will change over following weeks, Howell-Jolly bodies will appear



this is a matter of personal choice.

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Post-splenectomy changes

- Platelets will rise first (therefore in ITP should be given after splenic artery clamped)
- Blood film will change over following weeks, Howell-Jolly bodies will appear
- Other blood film changes include target cells and Pappenheimer bodies
- Increased risk of post-splenectomy sepsis, therefore prophylactic antibiotics and pneumococcal vaccine should be given.

Post-splenectomy sepsis

- Typically occurs with encapsulated organisms
- Opsonisation occurs but then not recognised

*usually from dog bites

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Vaccinations

It is important to be aware of vaccines which are of the live-attenuated type as these may pose a risk to immunocompromised patients. The main types of vaccine are as follows:

Live attenuated

- BCG
- measles, mumps, rubella (MMR)
- influenza (intranasal)
- oral rotavirus
- oral polio
- yellow fever
- oral typhoid*

Inactivated preparations

- rabies
- influenza (intramuscular)

Detoxified exotoxins

- tetanus

Extracts of the organism/virus (sometimes termed fragment)**

- diphtheria
- pertussis ('acellular' vaccine)
- hepatitis B
- meningococcus, pneumococcus, haemophilus

Notes

- influenza: different types are available, including whole inactivated virus, split virion (virus particles disrupted by detergent treatment) and sub-unit (mainly haemagglutinin and neuraminidase)
- cholera: contains inactivated Inaba and Ogawa strains of *Vibrio cholerae* together with recombinant B-subunit of the cholera toxin
- hepatitis B: contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology

*whole cell typhoid vaccine is no longer used in the UK

**may also be produced using recombinant DNA technology

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Tetanus: vaccination

The tetanus vaccine is a cell-free purified toxin that is normally given as part of a combined vaccine.

Tetanus vaccine is currently given in the UK as part of the routine immunisation schedule at:

- 2 months
- 3 months
- 4 months
- 3-5 years
- 13-18 years

This therefore provides 5 doses of tetanus-containing vaccine. Five doses is now considered to provide adequate long-term protection against tetanus.

Intramuscular human tetanus immunoglobulin should be given to patients with high-risk wounds (e.g. Compound fractures, delayed surgical intervention, significant degree of devitalised tissue) irrespective of whether 5 doses of tetanus vaccine have previously been given

If vaccination history is incomplete or unknown then a dose of tetanus vaccine should be given combined with intramuscular human tetanus immunoglobulin for high-risk wounds

Next question >

